



FIGURE 1A

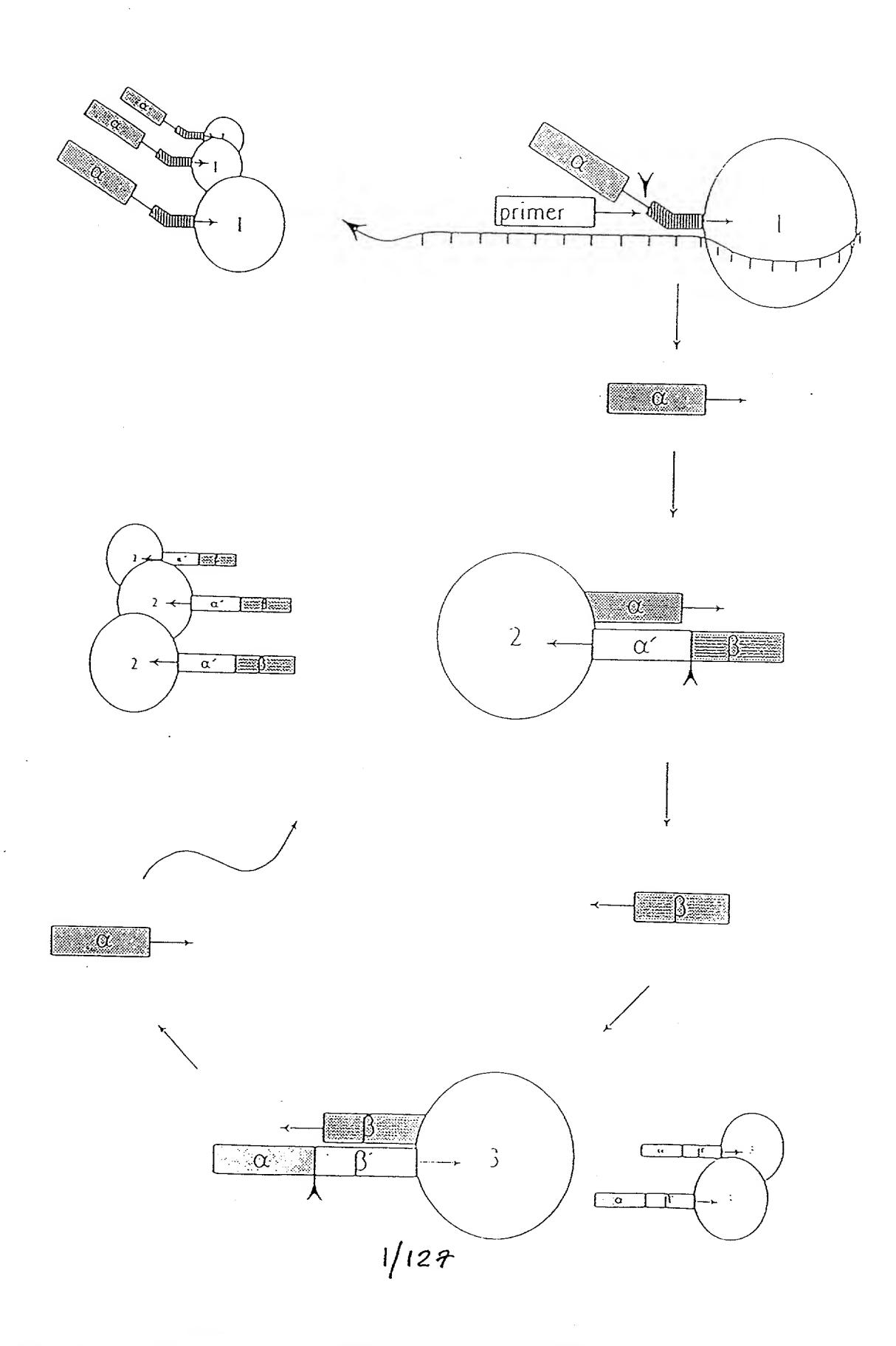
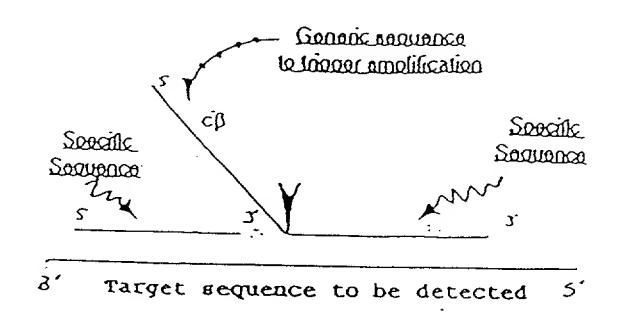
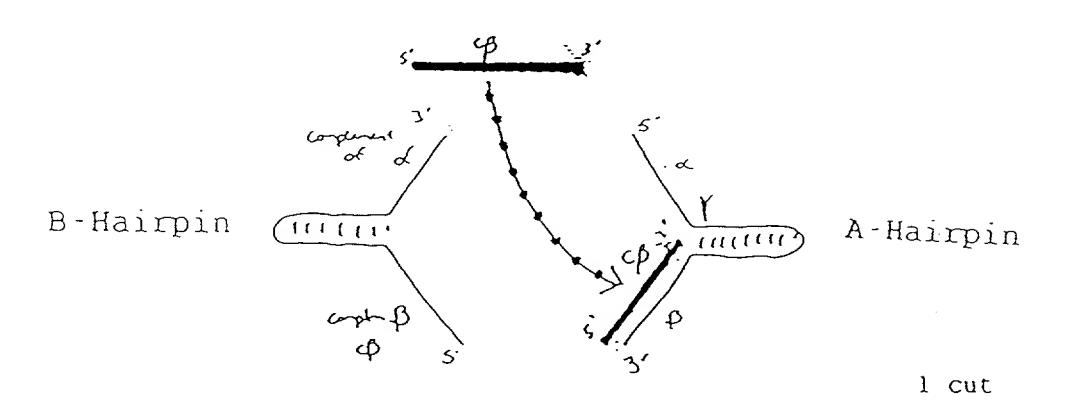


FIGURE 1B

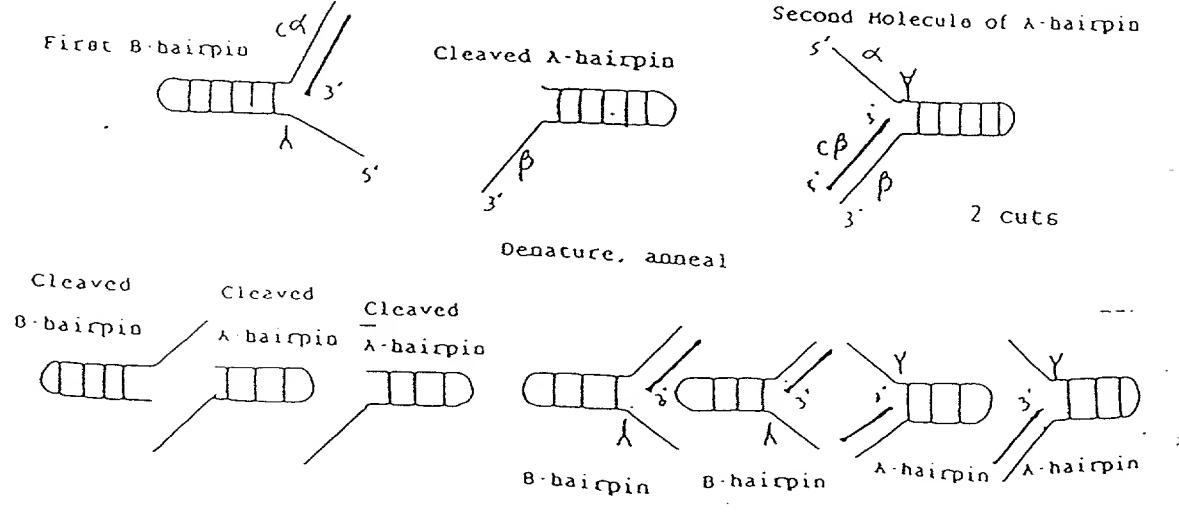
PART ONE: TRIGGER REACTION



PART TWO: DETECTION REACTION



Denature, anneal



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AI CXX C C C C C C C C C C C C T I T C A C C C C C A A G C C C C C T C C T C C T C C T C C C C	A G G G G G G G G G G G G G G G G G G G	G C C A A C C C C C C C C C C C C C C C	CA	CCCCTCXI CCT CCT IT CACCCAA		CGGGCCGGCCCCACCCGGGGGACTTT		CCIICCCCCCCCACCICCCCC	0
(SEO 10 NO:7)	(SEQ 10 NO:1) (SEQ 10 NO:2) (SEQ 10 NO:3)								
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FIGURE 2 (cont'd)

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(SEQ 10 NO.7)	(SEQ 10 NO:1) (SEQ 10 NO:2) (SEQ 10 NO:3)					•			
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FIGURE 2 (cont'd)

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(SEQ 10 NO:7)	(SEQ 10 NO:1) (SEQ 10 NO:2) (SEQ 10 NO:3)	-							
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	1111		1184 1181 1180		12 S 12 S 12 S		132		138
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(SEQ 10 NO:7)	(SEQ ID NO:1) (SEQ ID NO:2) (SEQ ID NO:3)					•			-
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MAJORITY		CAAGAACACCTACATXG
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NAJORITY		C C C C C C I I C A A C C A C C C C C C
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180 180 181(

MAJORITY	(SEQ IO NO:7) A	GAACAI CCCCCI C C C C C C C C C C C C C C	
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MAJORITY	O	GCCCA	(2)
OKAPTAD CKAPTR CKAPTR KTPAPC		C	1884 1881 1890
, MAJORITY	Ø	AI CCGGGICII CCAGGGGGGGGGGACAI CCAGACCCAGGCGGCGGGGGGGGGG	
ONAPTAD CNAPTR CNAPTR		6	1984 1981 1980
MAJORITY.	Q	GGCCGTGGACCCCCT	
ORAPTAD A WPTR CRAPTTH		A. G. G	2021
MAJORITY	O	CACCCCICICCCAGGAGCTICCCATCCCCIACCAGGAG	O
ONAPTAD CNAPTR CRAPTR	· -	T	209 209: 2100

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	2161		2234 2231 2240		2304 2301 2310		2371		2444 2441 2450
ACCTICCCCAAGGIGCGGCCTGGATIGAGAGACCCTGGAGGGGGGGGGG	A A A B C C C C C A C C C C C C C C C C	CCCIACGI	C	C C C C A I C C C C C I C A C C C C C C		0 0 0	A 6 G	CCAAAGACCGGGCGCAGGXGGTGGCGGCTTTGGCCAAGGAGGGTCATGGAGGGGGGGGG	β
(SEO 10 NO:7)	(SEQ ID NO:1) (SEQ ID NO:2) (SEQ ID NO:3)								
MAJORITY	OKAPTAD CKAPTH CKAPTH	MAJORITY	ONDOTADO CRAPTA CRAPTA	MAJORITY	ONDPIED CHAPTH CHAPTH	MAJORITY	OKAPTAD CKAPTA CKAPTA	IADORITY	OHAPTAD CHAPTH CHAPTH
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MAJORITY (SEQ 10 NO:7) CCCCCTCCAGCTCGAGGTGGGGGGGGGGGGGGGGGGGGG	0 (SEQ IO NO:1)	(SECTIONO:2)	(SEO O OES)	(SEO 10 EQ 10 1 EQ 10 1	(2	0 6 6 6 4 6 6 4 6 7 6 6 6 7 6 7 6 6 6 6 6
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MAJORITY (SEQ 10 NO:8)	MX A ML PLF E PKGRVLLV OGHHLAYRIFFALKGLIISRGE PV OAVYGFAKSLLKALKE OG. OAVXVVF OAK
120 PRO (SEO 10 NO:4) TR PRO (SEO 10 NO:5) TR PRO (SEO 10 NO:5)	B C
MAJORITY	KAGRAPIPE OF PROLALI KELVOLLCL XRLE VPGY EADOVLATLAKKA EK EGY EV
24 FR	S
MAJORITY	RI AVL HPEGYLI TPAWLWEKYGL RPEOWVOYRAL XGOPSOHLPGVKGI GEKT
74 750 77 750 77 750 77 750	8
MAJORMY	KI XAHME OLXL SXXL SXVRIOLPLEVOFAXRREPOREGLRAFL
140 PR0 FR PR0 FR PR0	
MAJORITY	PKALEEAPWPPPECAF VGFVLSAPEPM WAEILALAAARXGRVHRAXOPLXGIROLK
14 780 17 78 781 18 780 18 780	

4 2 0

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88 88 70

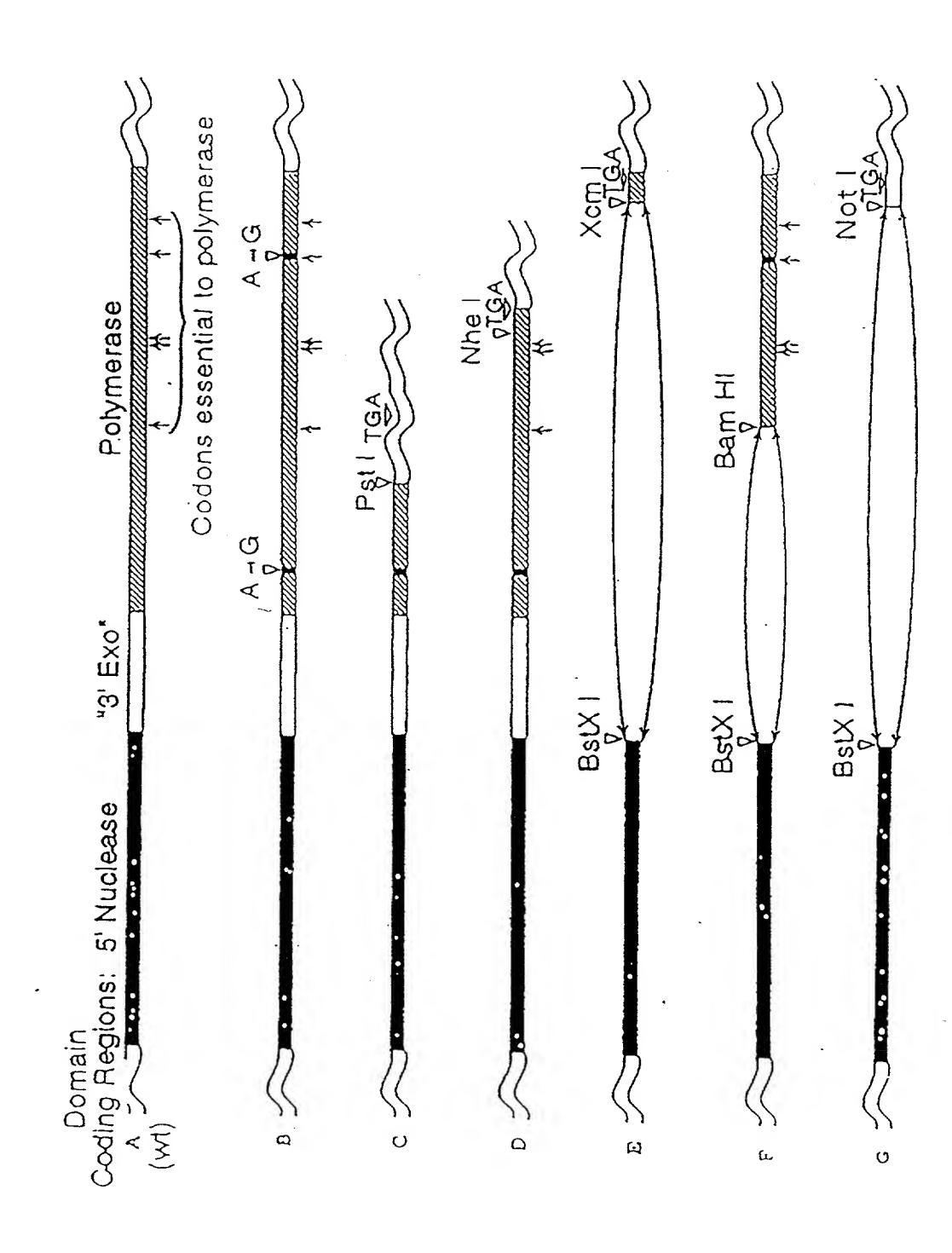
MAJORAMY (SEO 10 NO:8)	RCLIAKOLAVLALREGLOLXPGODPHL LAYLLOPSHII PEGVARRYGGEWIE OAGERALLSERLFXHEA	
IAD PRO (SEQ ID NO:4) IR PRO (SEQ ID NO:5) ITH PRO (SEQ ID NO:6)	β	< \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \
MAJORITY	E K P L S R V L A H M E A T G V R L O V A Y L O A L S L E V A E E I R R L E E V F R L A G	
120 PR 0 17 PR 0 17 PR 0 17 PR 0	K. K	ব ব ব
MAJORITY	EKILOYRELTKLKHTYIOPLPXIVHPR	
120 PR0 TR PR0 TR PR0	S	<i>(</i>) () ()
. MAJORMY	RIHTRFHOTATATCRISSOPHLOHIPVRTPLCORIRRAFVAEECWXLVALOYSOIELRVLAHISCO	
120 PR0 PR PR0 PR PR0		
IMORT	LYGMSAHRLSOELAI PYEEAVAFIER	
140 PR0 PR PR0 PR PR0	S	

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FIGURE 3 (cont'd)

MAJORITY (SEO ID NO:8)	SF PKV RAYI EKTLEEGRRRGYVETLF GRRRYV POLHARVKSVREAAERMAF KMP V OGTAAOLMK LAMVKL
120 PRO (SEO 10 NO:4) 17 PRO (SEO 10 NO:5) 17 PRO (SEO 10 NO:5)	2
MAJORITY	F P R L X E MG A R MI L OV H D E L V L E A P K X R A E X V A A L A K E V ME G V Y P L A V P L E V E V G X G E O W L S A K E X
18 80 88 87 18 88 18 88 18 88	8 B B B B B B B

767 785 770



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Genes for Wild-Type and Pol(-) DNAPTH

43' EXO*

Domain
Coding Regions: 5' Nuclease
(wt)

Polymerase

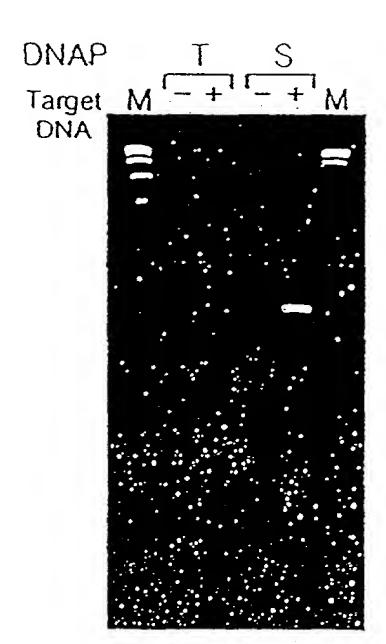
Codons essential to polymerase

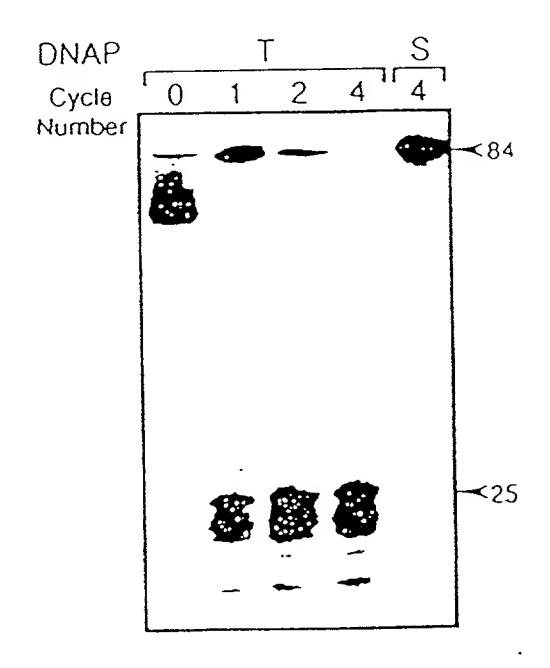
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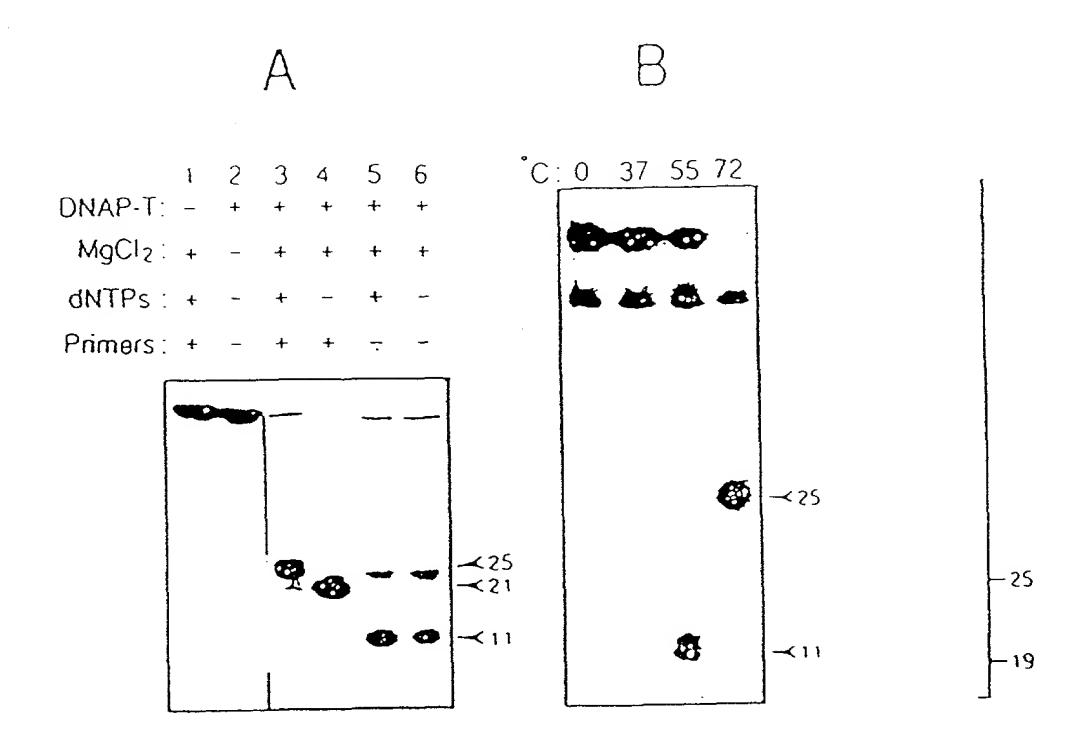
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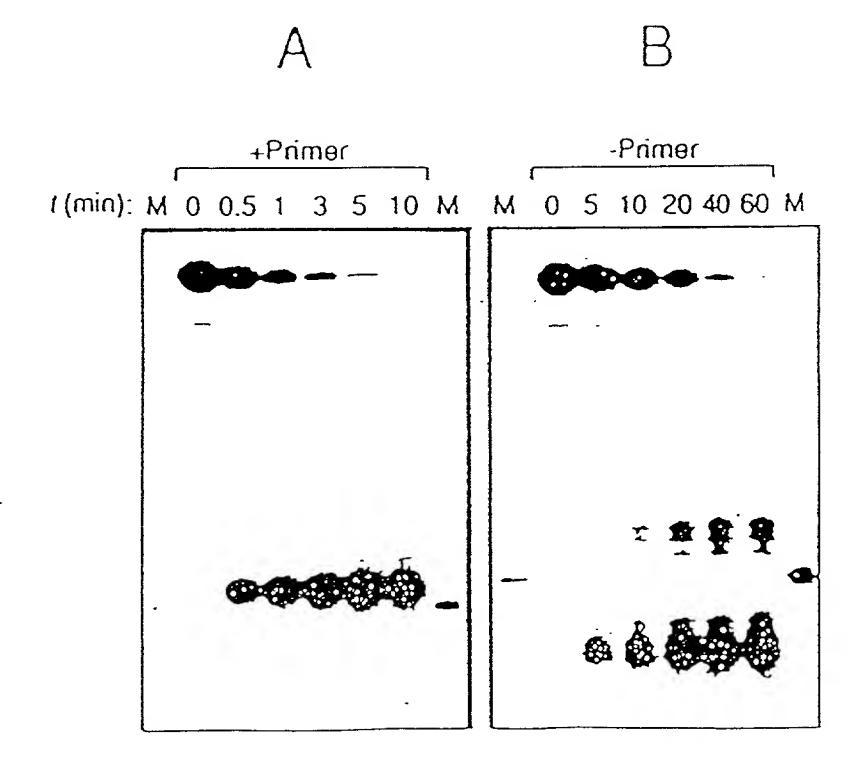
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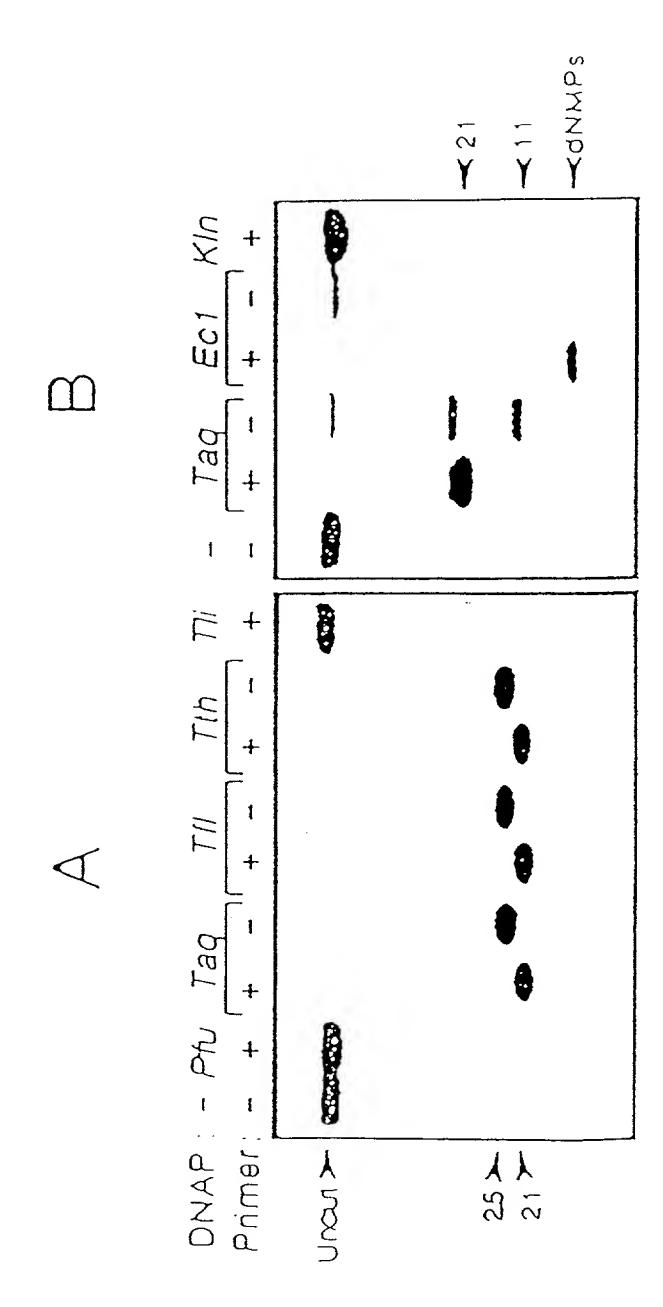






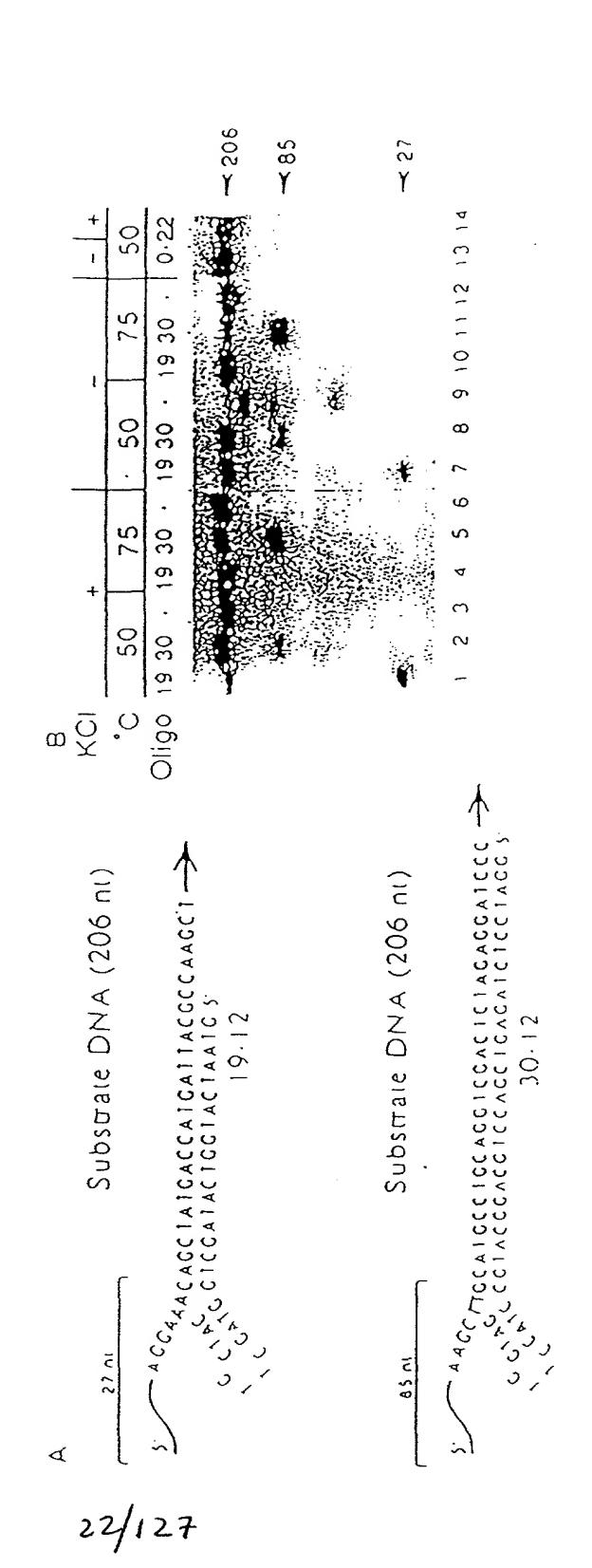


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FIGURE 12



30.0 ω

> AACCUCCAUCCCUCCACUCUAGACGAUCCCC Substrate RNA (46 nt)

-35 Tigacaattaacaatticaicgidilaigigigigigaattigigagegegataacaatticacaeagaaacageg

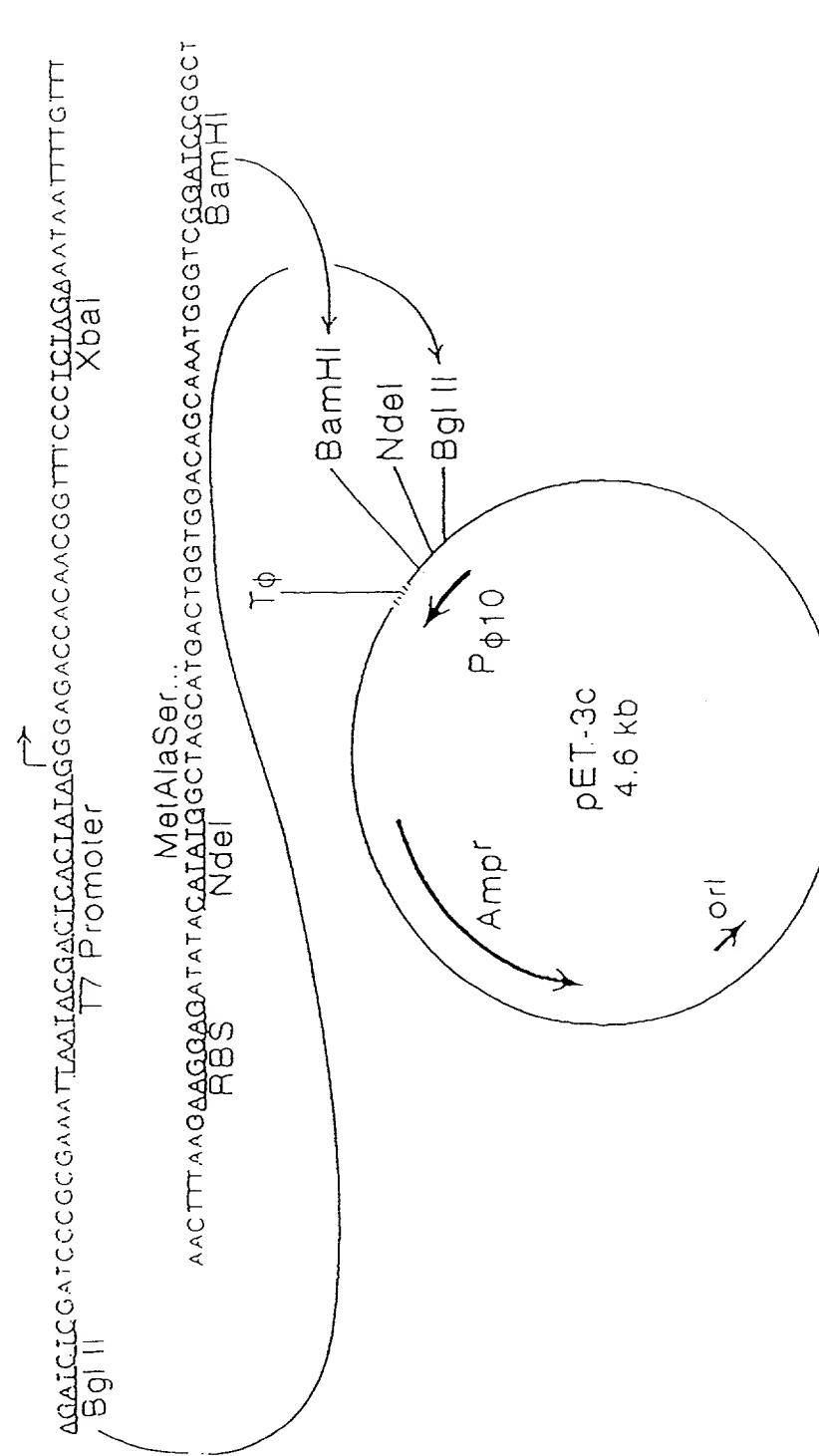
HindIII Pst 1ac 19 lacZ Xbal pTTQ118 4563 b.p. ptac Amp^{Γ} Smal Sstl

ABS: Ribosome binding sile

Synthetic tac promoter plac:

lac 10: Lac repressor gene

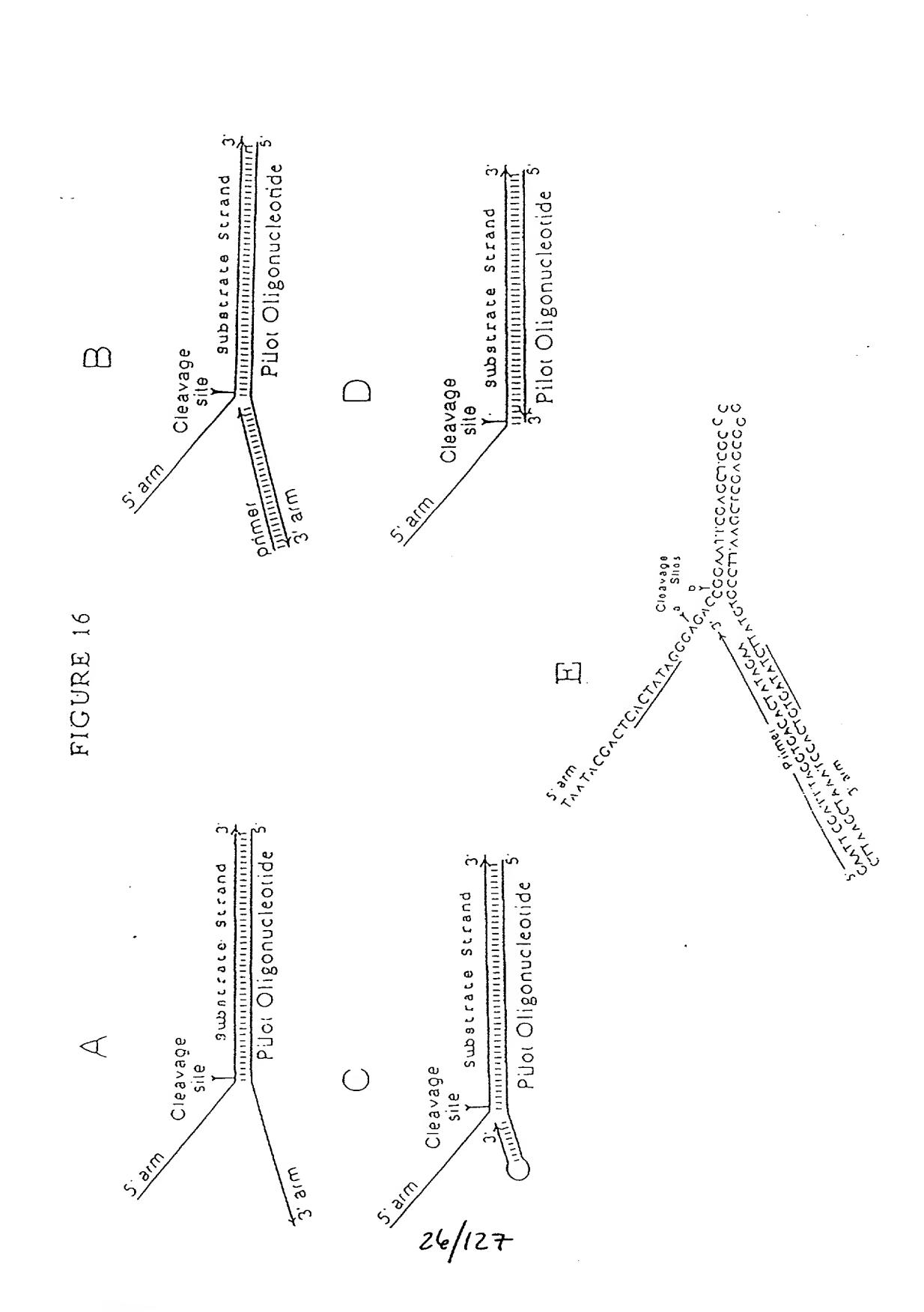
E. coli rrnB transcription terminator Bela-galactosidase alpha fragment rrnBl: lac2:



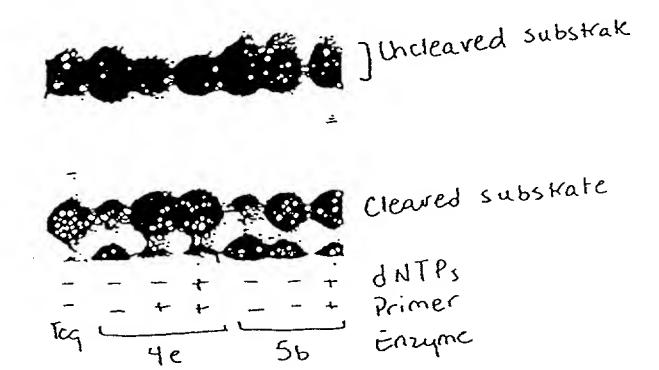
Ribosome binding site RBS: Bacteriophage T7 #10 promoter

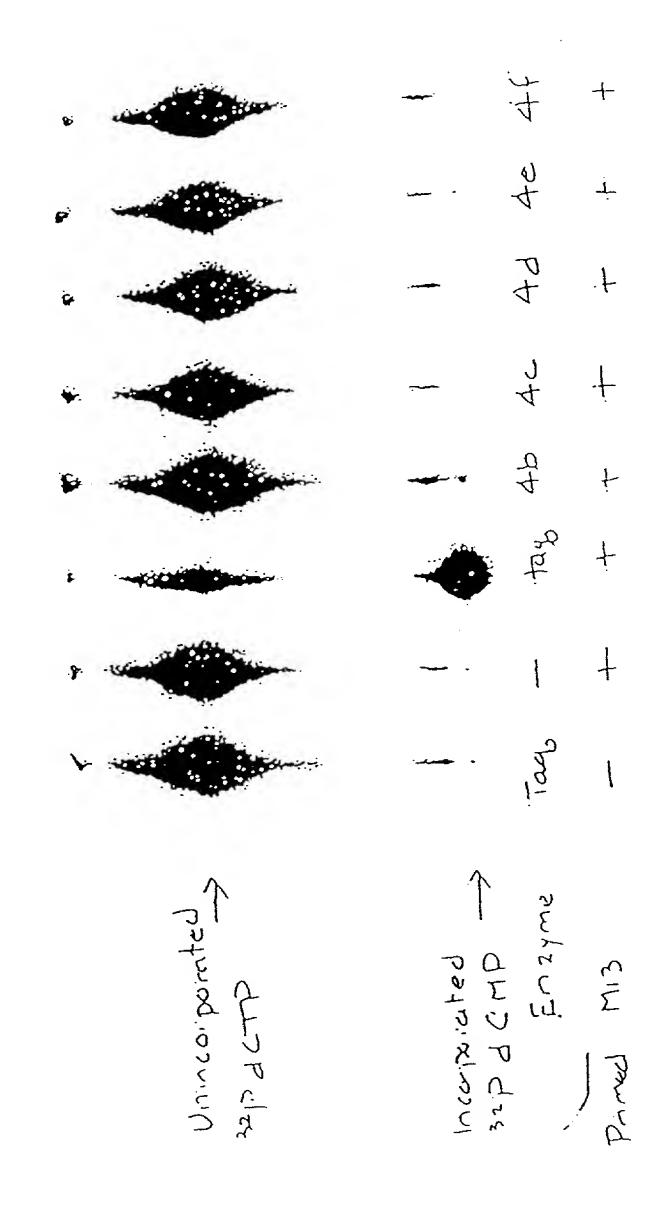
P. ф 10: T. ф: T. 7

Terminator



1 2 3 4 5 6 7





A

(32p) TAATACCACTATAG SILES OF CLEAVAGE

With a

With a

ST

GATTTAGGTGACACTATAG

CACTATAGGTGACACTATAG

CATTAAGCTAAATCCACTGTGATATCTTATGTGCCTTA

A

GATTTAGGTGACACTGTGATATCTTATGTGCCTTA

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GATTAGGTGACACTGTGATATCTTATGTGCCTTA

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Travel by polymenzation

Some abordant charage with 46" because of recidial polymerase activity

A			Predicted cleanage
S' CCGACGANCAAGCGAGAG			1 sites
Tau" CALACACGZCACAGCAGAGA 3'	CATGC A AGAACCCACAE 7	A-Hairpin	
S'CTTTCTCCCTGTCTCCTCTCT "MIPHA"CTCCTTGTTCCCTCTC	CTACC T	T- Hairpin	
·	t alpha primer	3 ·	
C Tav"	S' XCACACI A GTACC C CATGC A	رداوha" CTGCTTGTTCCC	COTOTOL A CATGO S TOTOTOTOTOTOTOTOL CATGO S
3' CAAKGACGACAGCAGAG	Agracocacas T	_	T- Hairpin
D		•	
	Fisa I M	NIS III	
Top = T-Hairpin	n BsmAi	HgiC I NIa IV Rsa I Kpn I	Bamal
C1:1C1C(1C1C:CC1C	::C:C:::GCC::C::G!\CC4;	GIGGIACCIGIGICGCIG	1(1(6(116116616
(30/127	CECCATCCAC 4C ACCG4C	ACAGEGRAC ANCERGEE

Ban H X TTAACATTATGCTGAGTGATATCCCGCTTAAGCTCGAGCCATGGGCCCCTAGGAG A A TIGIA A LACGACICACIA TAGGGCGGA A TICGAGCICGGIACCCGGGGA TCCIC ATCICAGCICGACGICCGIACGIICGAACICAIAAGATAICACAGIGGATITAICGAACCGCATTAGTACCAGTATCGACAAAGGACACACACTTAACAA PUOL 30-0 PUOL FACACICCACCICCACCCATGCAAGCIICAGIA. IICIAIAGICICACCIAAAIAGCIIGGCGTAAICAIGGICAIAGCIGIIICCIGIGIGAAIIGI Xpol Xmal Smal A v a | Asp Ban II Sst 1 п Сол COCCAGGG 1171CCCAG TCACGACGITGIAAAACGACGGCCAGIG GCSG1CCCAAAAGGG1CAG1GC,1GCAACA11111GC1GCCGG1CAC BspM | Sph | Hind || or so -1 Forward Acc -Hinc = Sall 31/127

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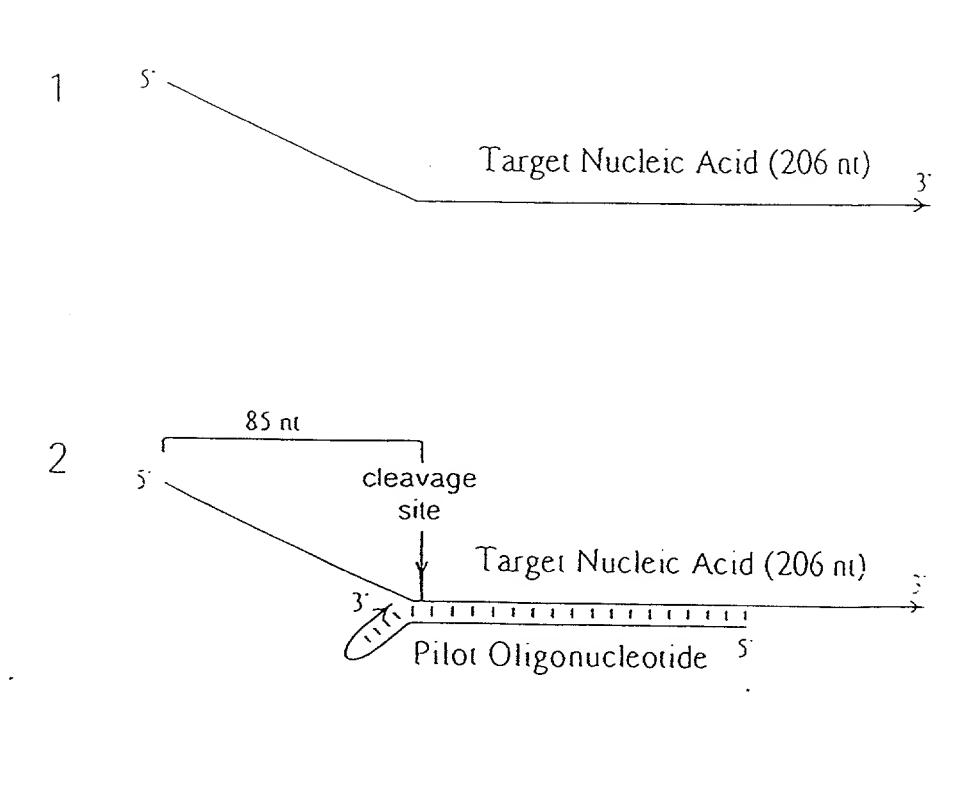
SICTIAACCICTCTATCT

206

48 7.5 C AC

ICCSC JE AC AAIICC AC AC ACA ACA

FIGURE 22A



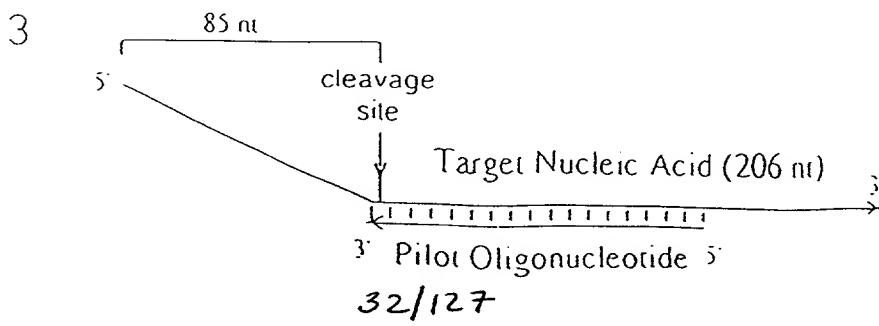


FIGURE 22B

$$\frac{1}{1} \frac{\pi}{2} \frac{\pi}{3} \frac{\pi}{1} \frac{\pi}{2} \frac{\pi}{3} \frac{\pi}{1} \frac{\pi}{2} \frac{\pi}{3} \frac{\pi}{1} \frac{\pi}{2} \frac{\pi}{3} \frac{\pi}{1} \frac{\pi}{2} \frac{\pi}{3}$$

$$\frac{206}{10} = \frac{1}{10} \frac{\pi}{10} \frac$$

CGAGACAGCG <u>.</u> CACCAA 5 - FL $\dot{\sim}$

S FL GROONAGNOCONGACAGG

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∞ - P;



$$=$$
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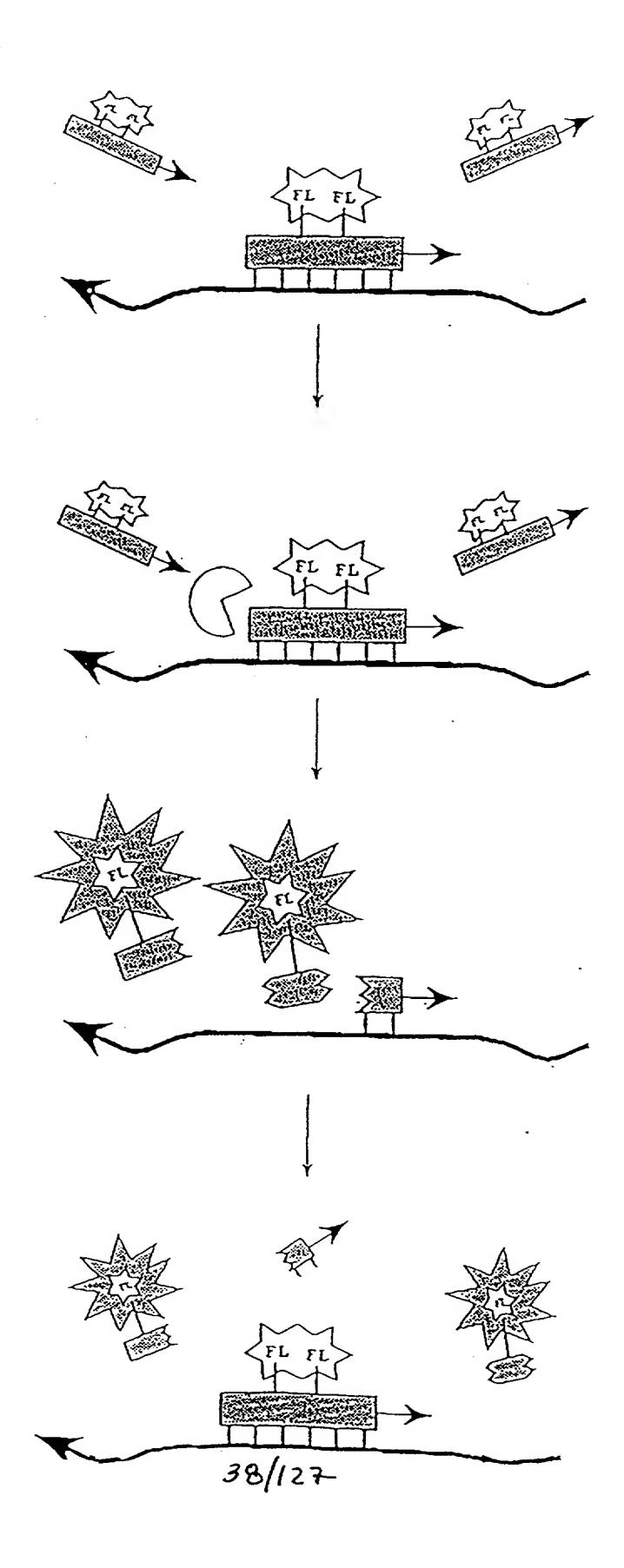
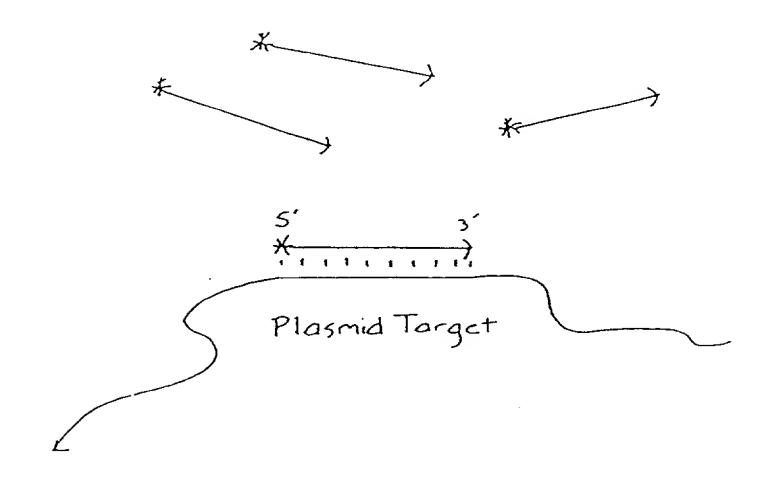


FIGURE 28A



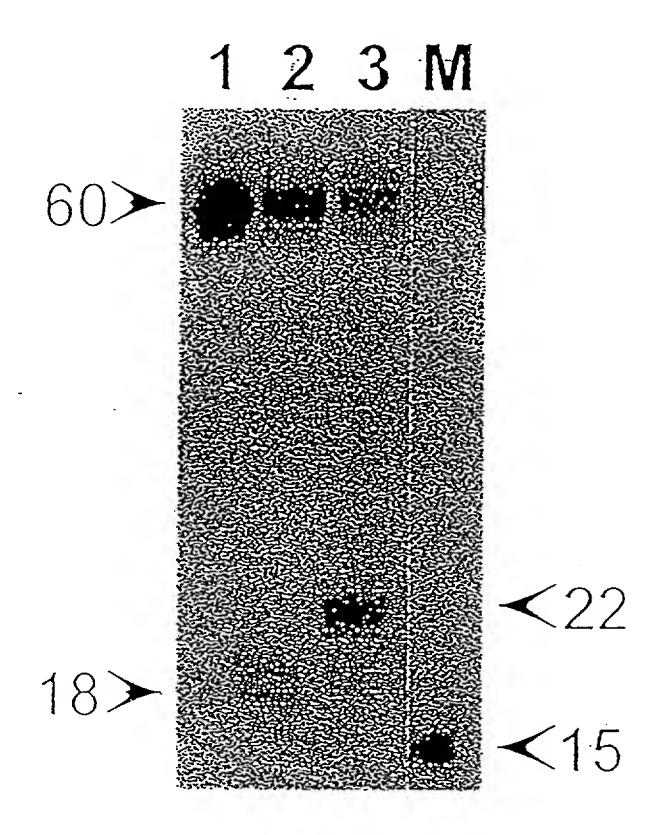
+ = 32 P 5' terminal phosphote

FIGURE 28B

M 1 2 3 A 5 6

 $\tilde{\Omega}$

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FIGURE 32

 $\hat{\Omega}$ AGAAAGGAAGGAAAAAGCGAAAGGF1uor Acccctttttcttcttttctttc Target Nucleic Acid ပ်-ပုက် ပ-ပ

AGCGGCGAACGTGGCGAGAAGGAAGGAAGAAGCGAAAGGFTuor. CTGCCCCT

 $\tilde{\Omega}$

t Nucleic Acid Target der" of 5' TGGCGAGAA

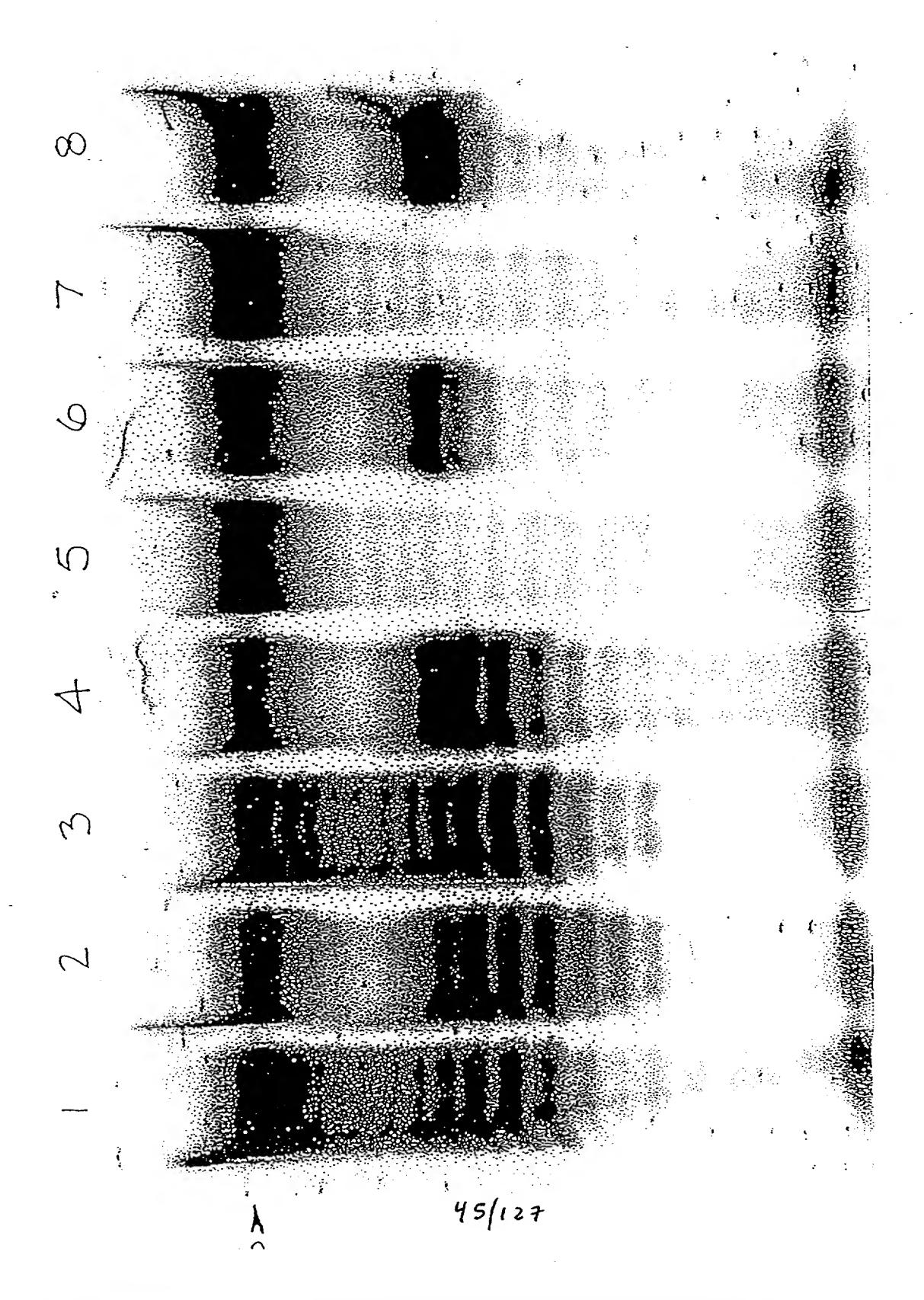
Ŝ ACCGCTCT CTGCCCCI

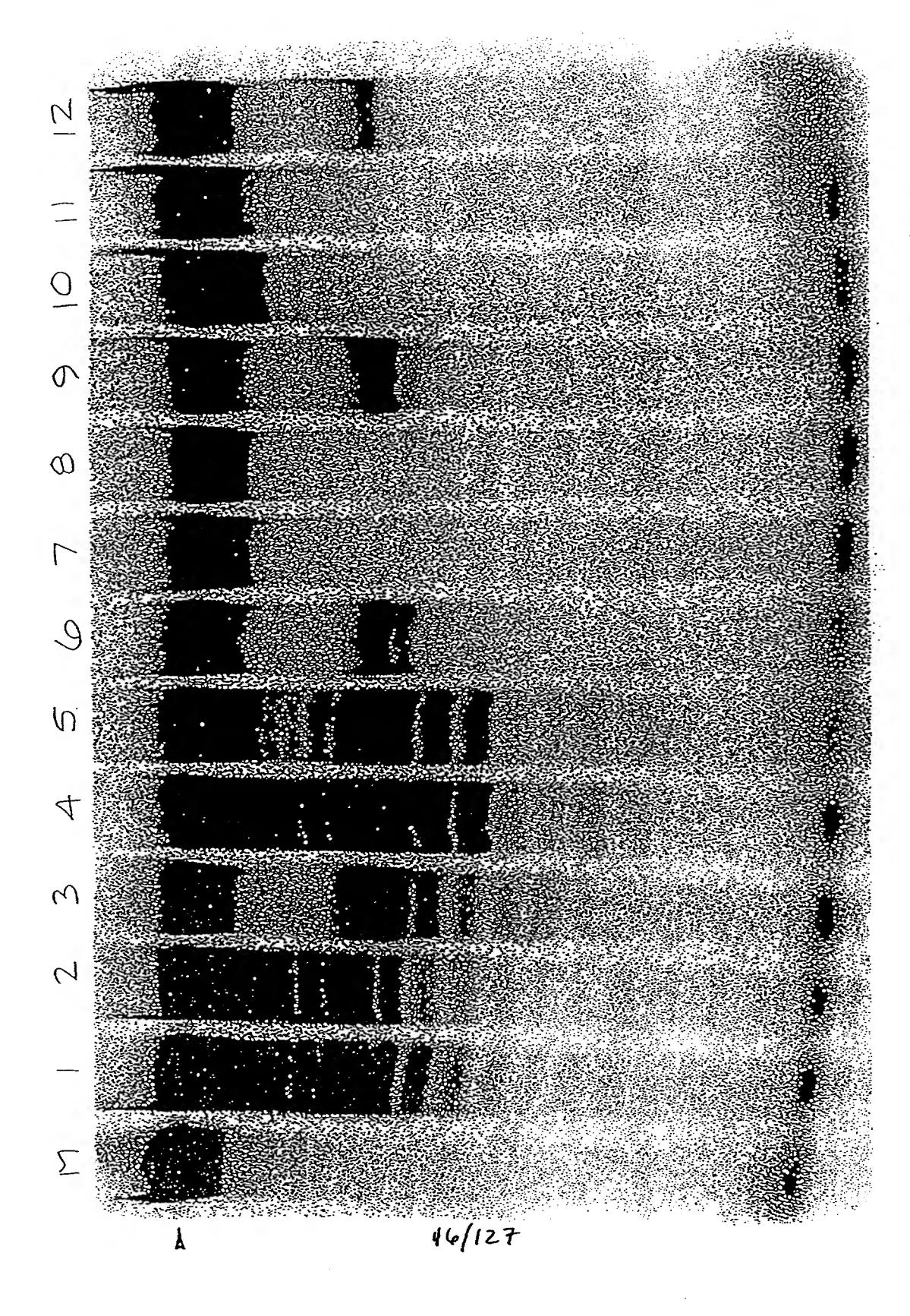
Target Nucleic Acid

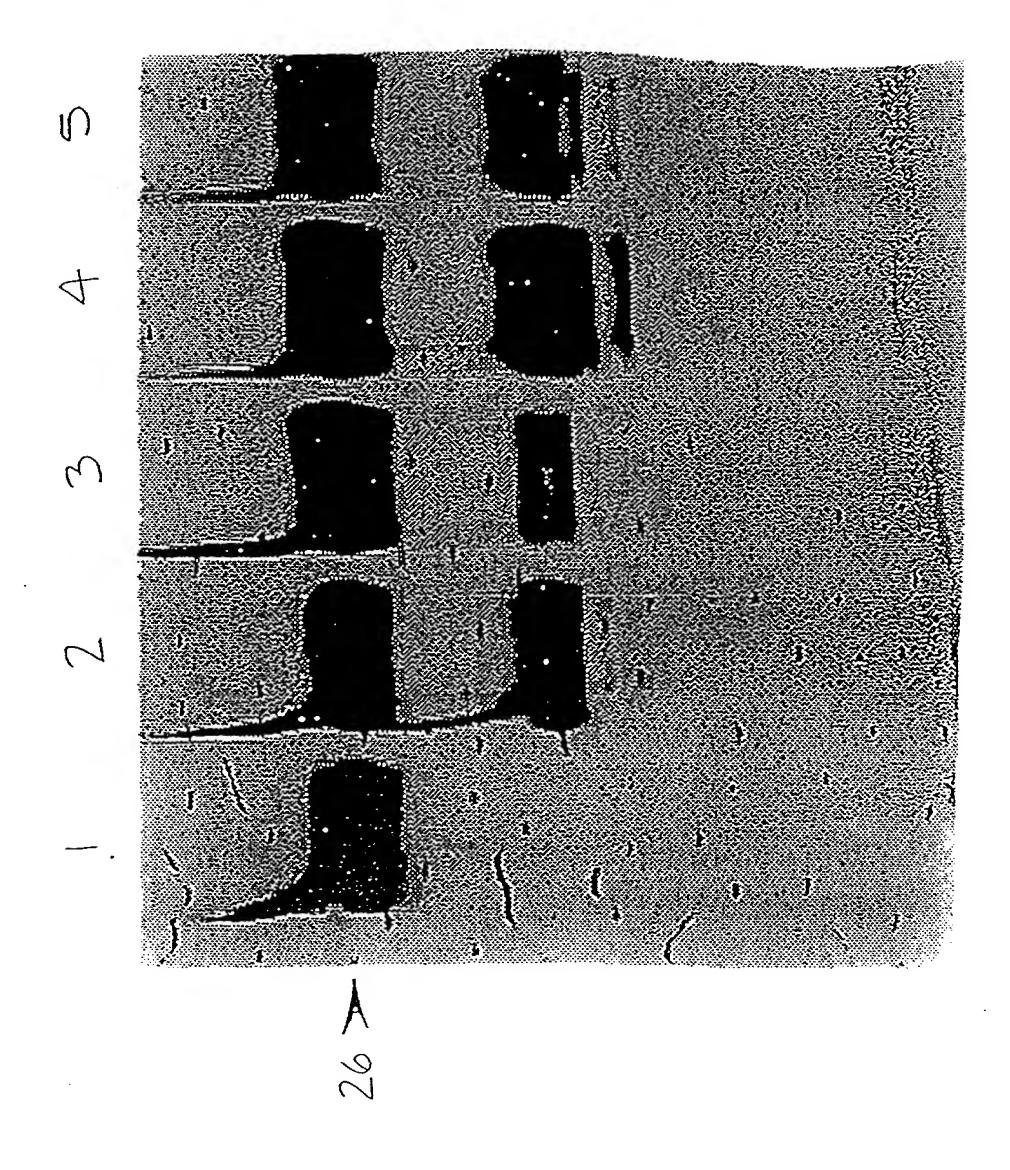
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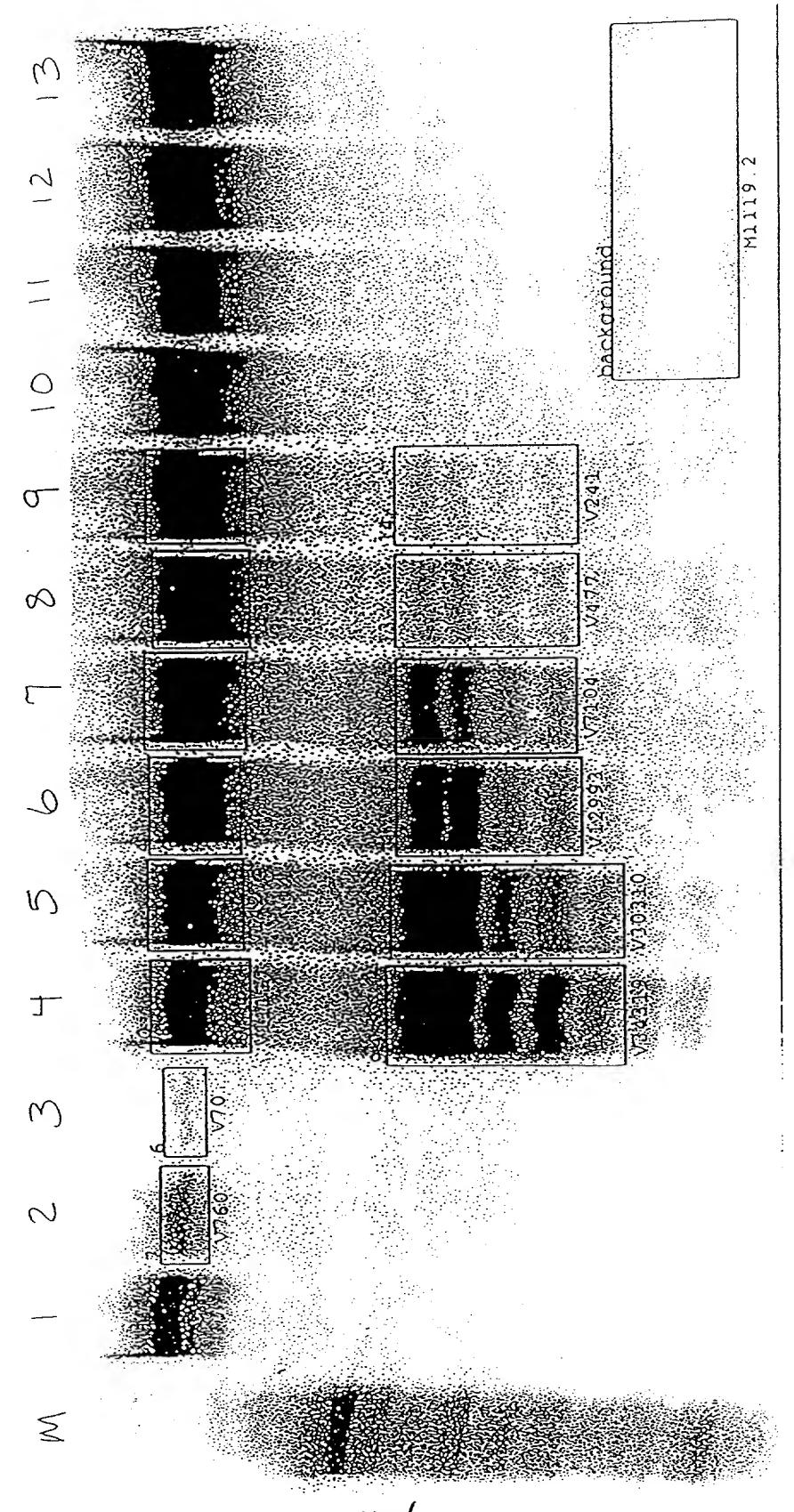
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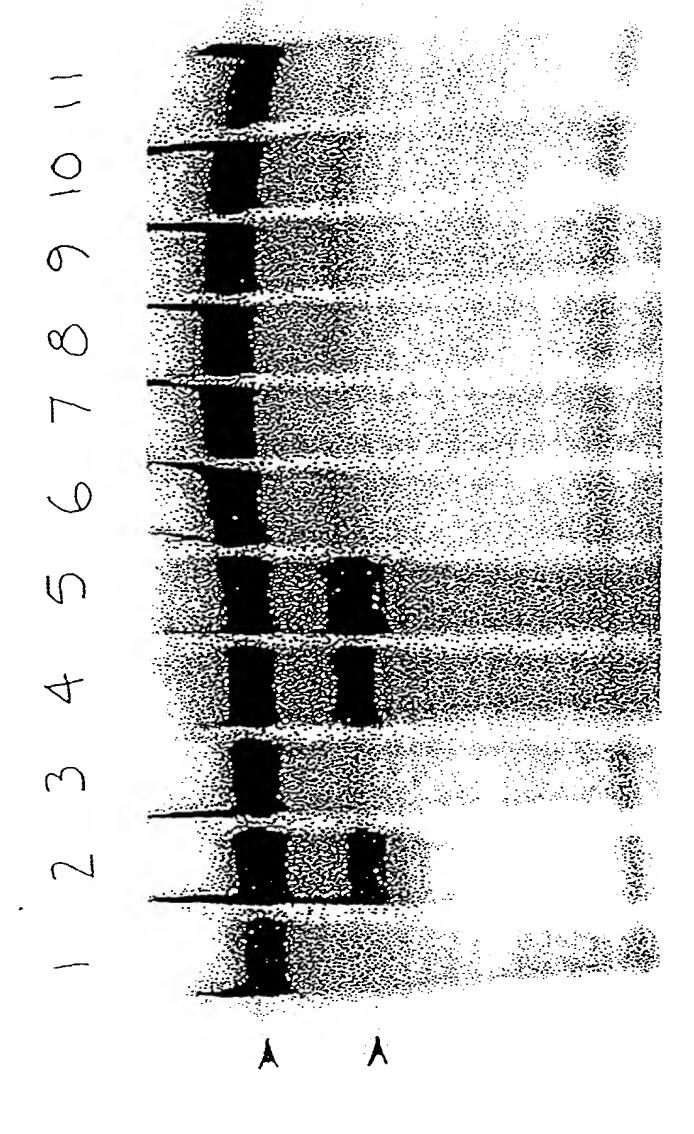




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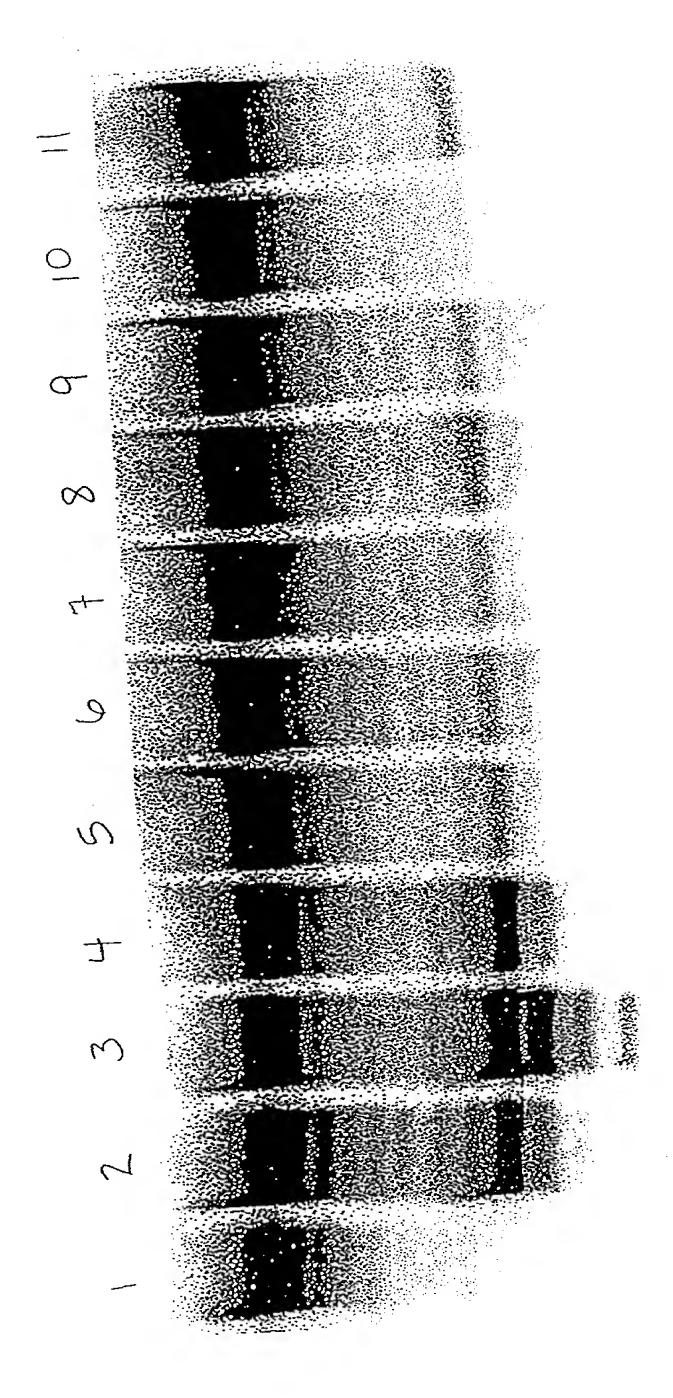


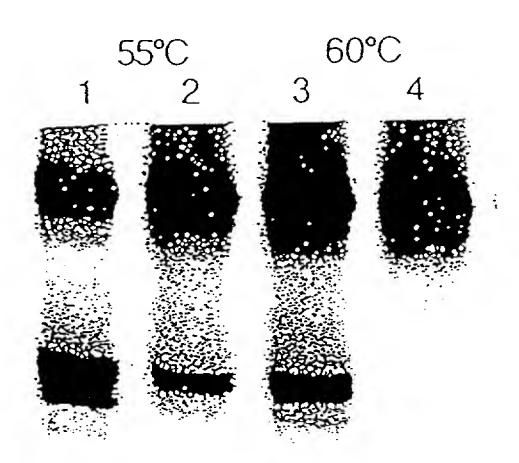
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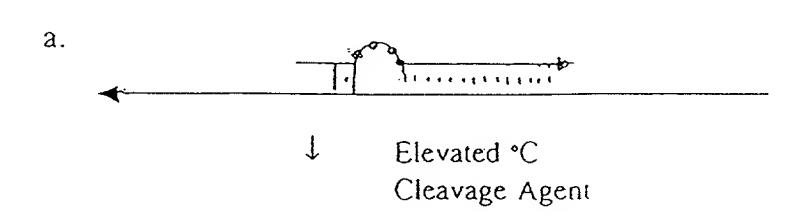


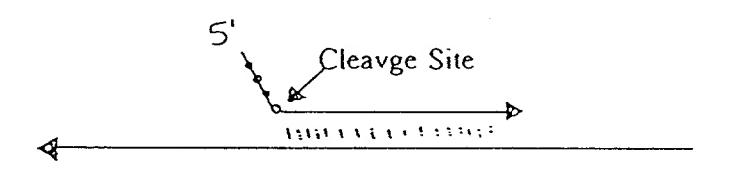
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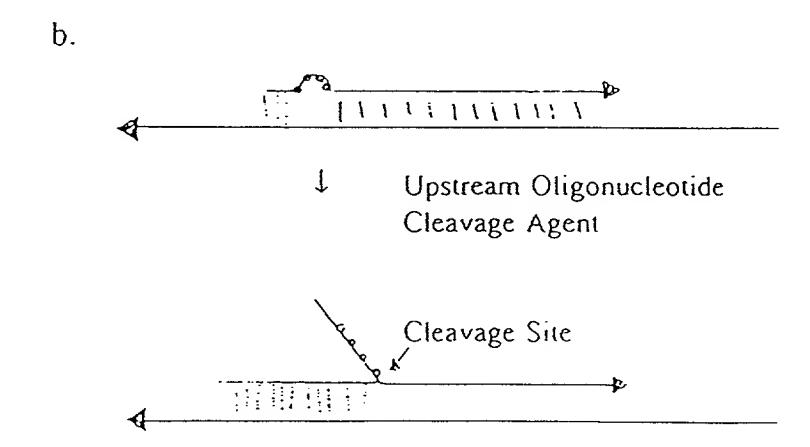












Invasive Cleavage Directing Oligo

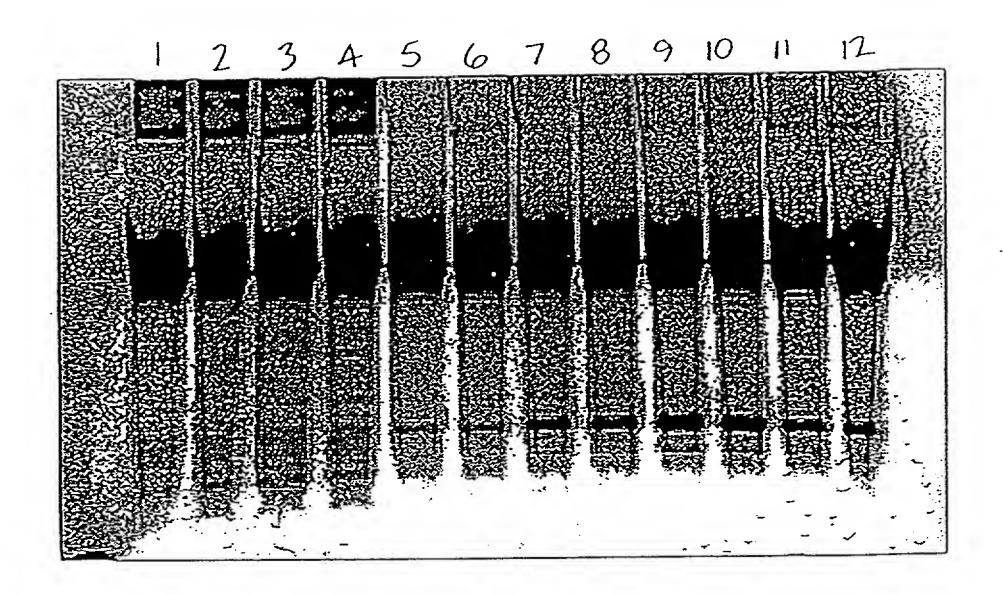
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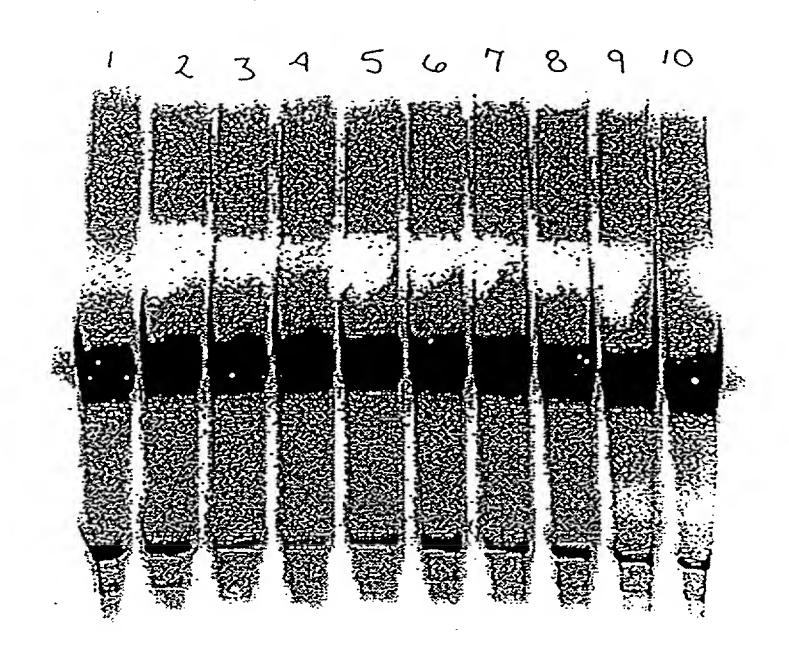
- Probe oligo

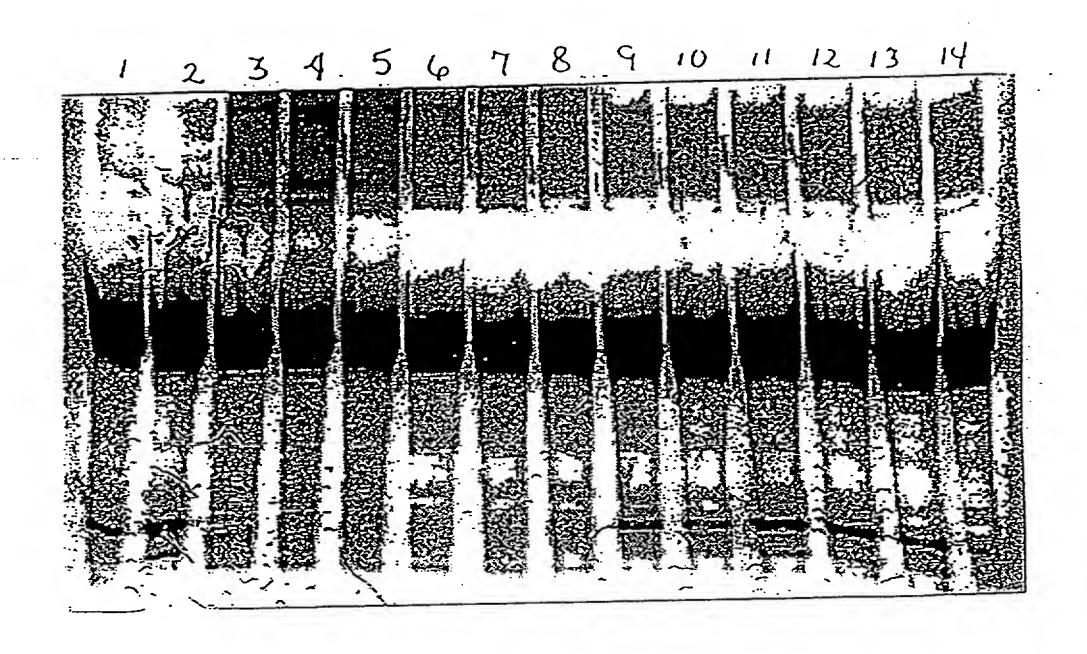
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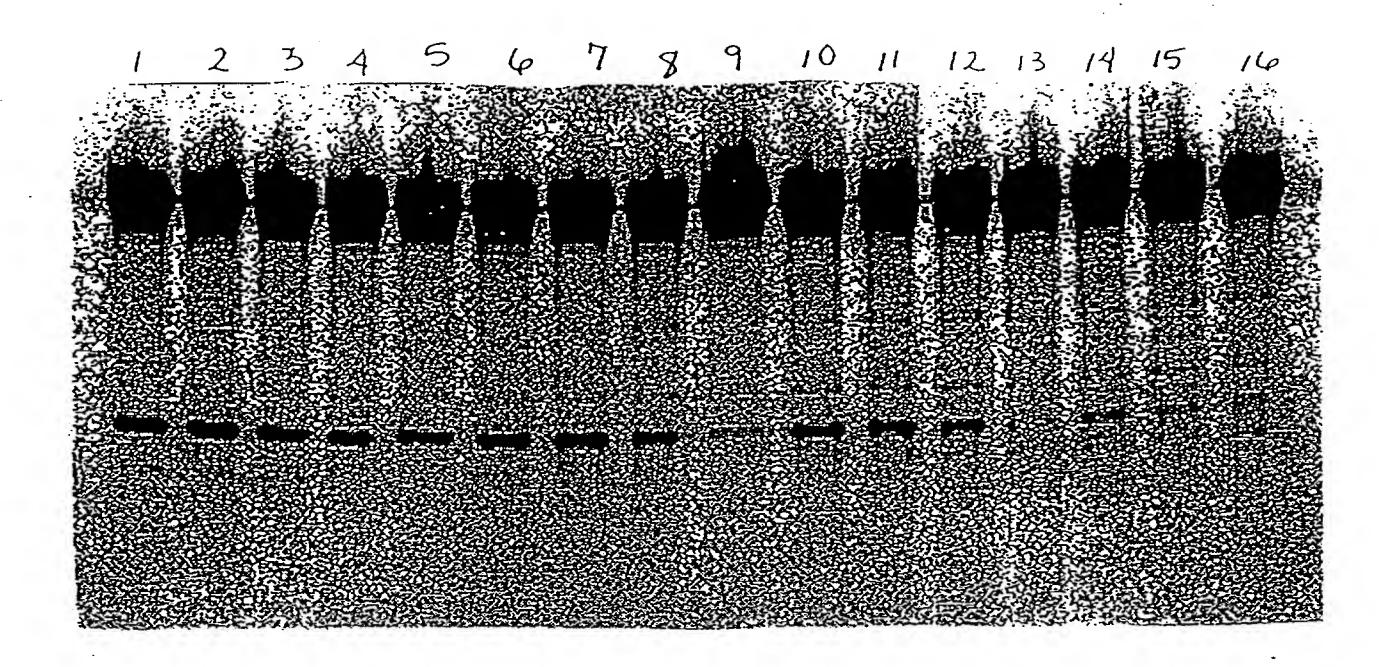
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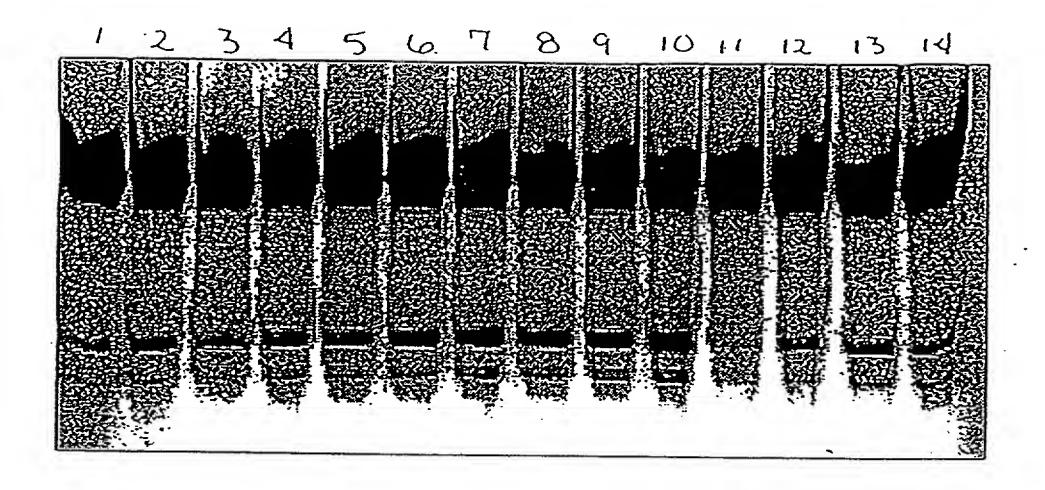
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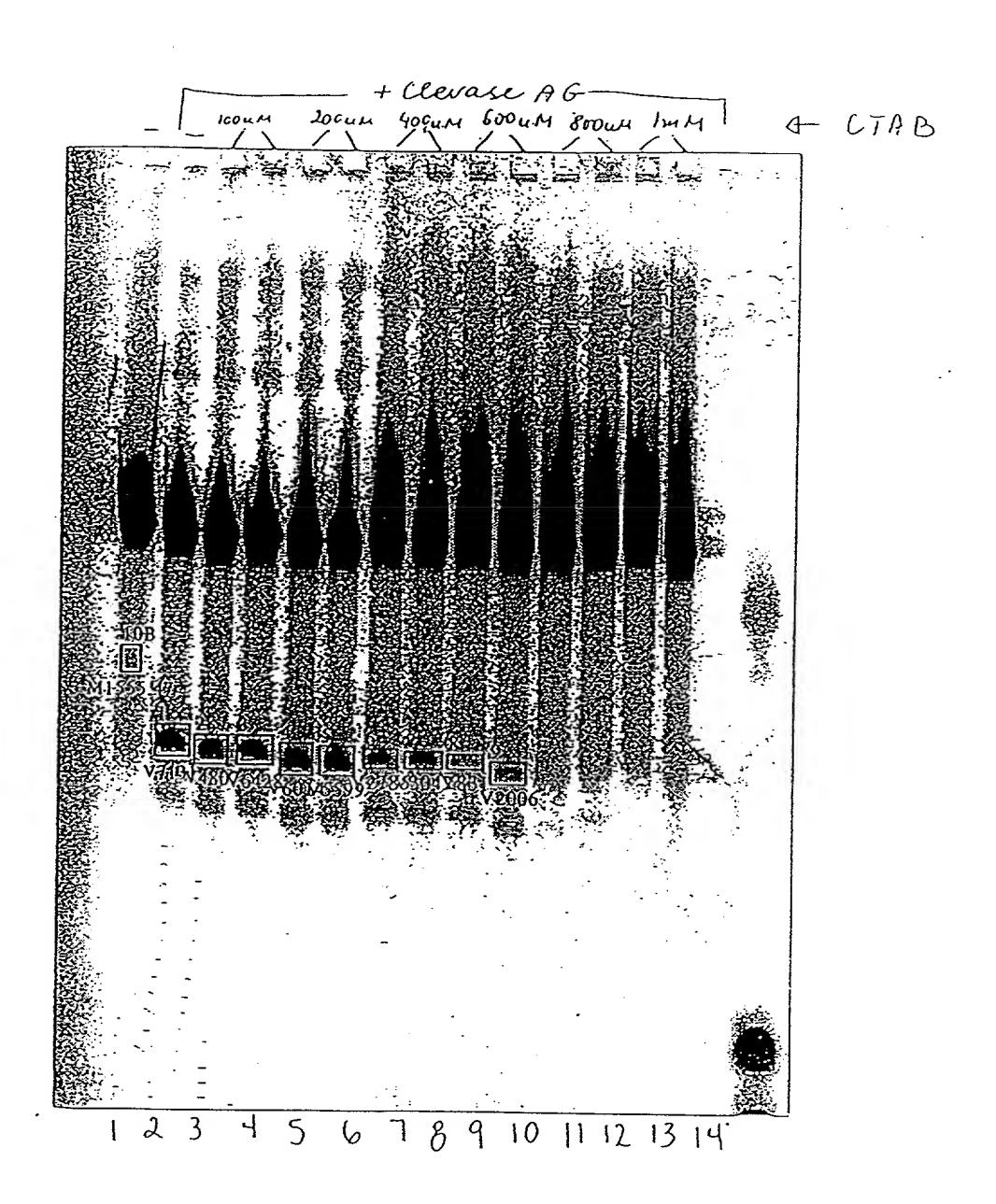




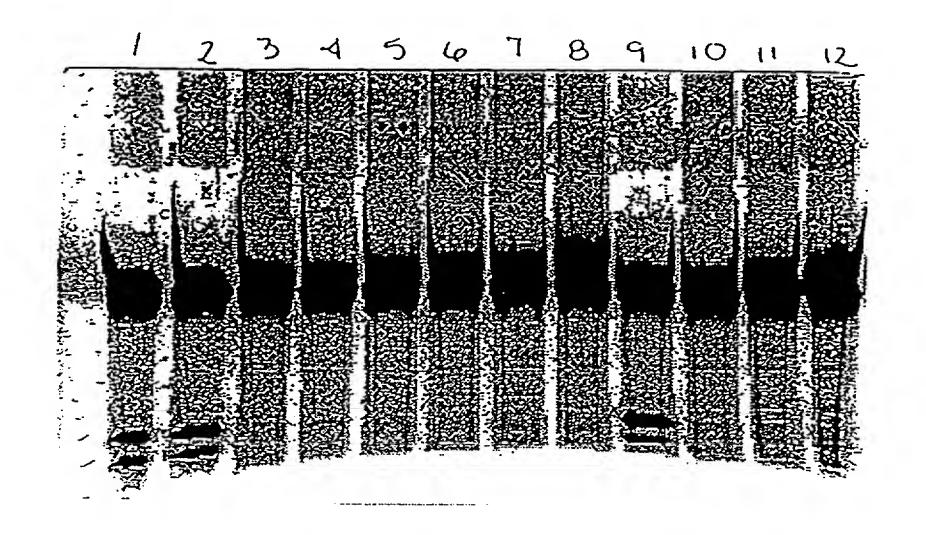


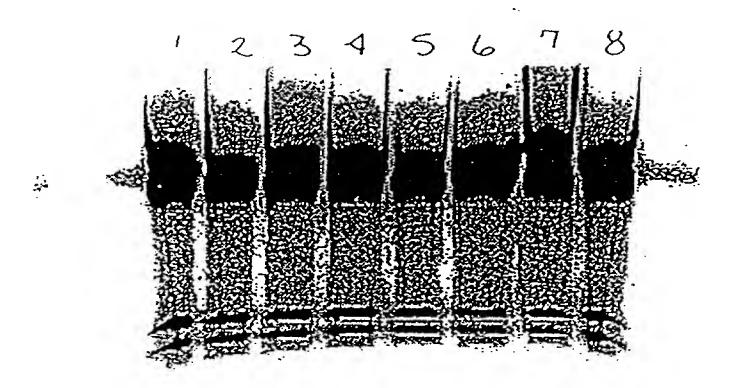


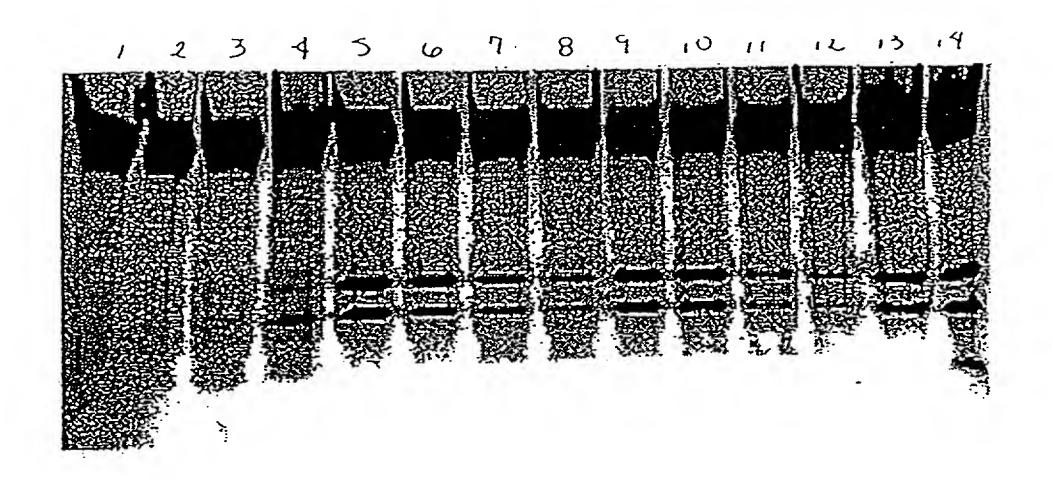


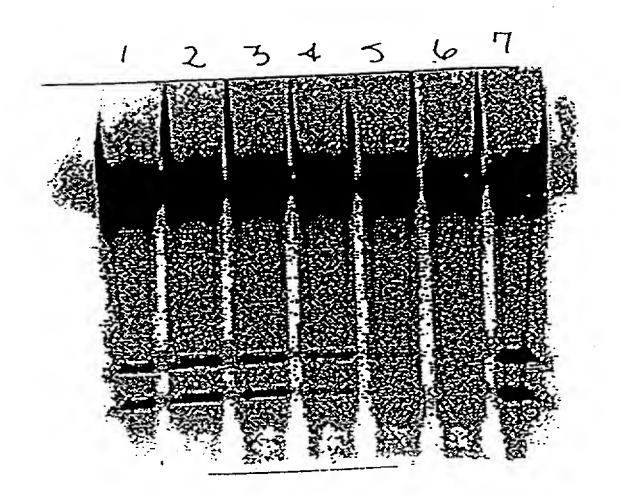


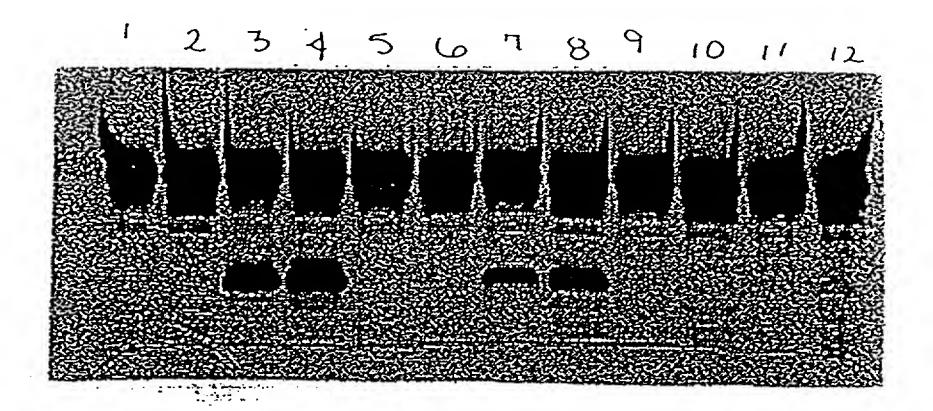
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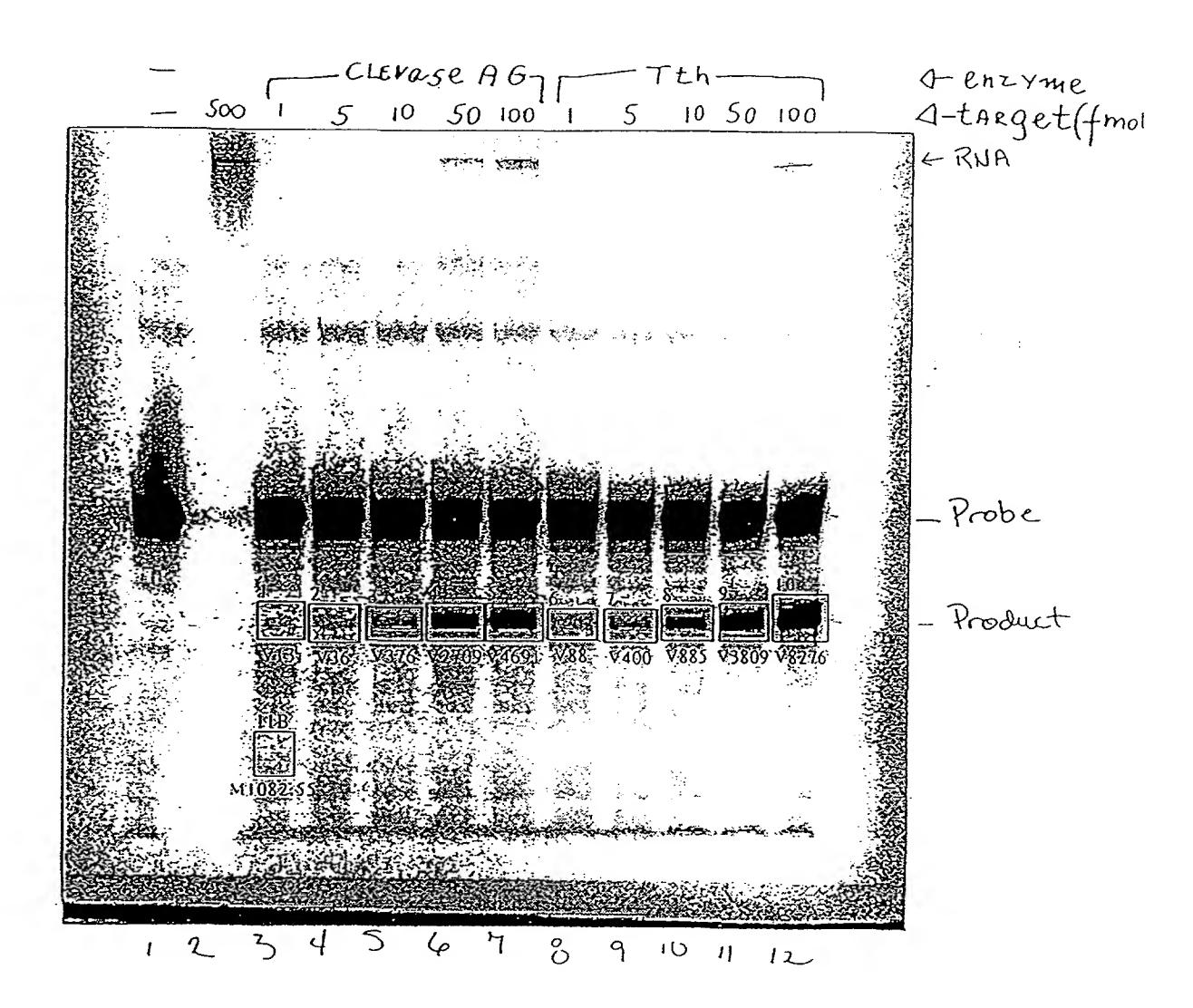




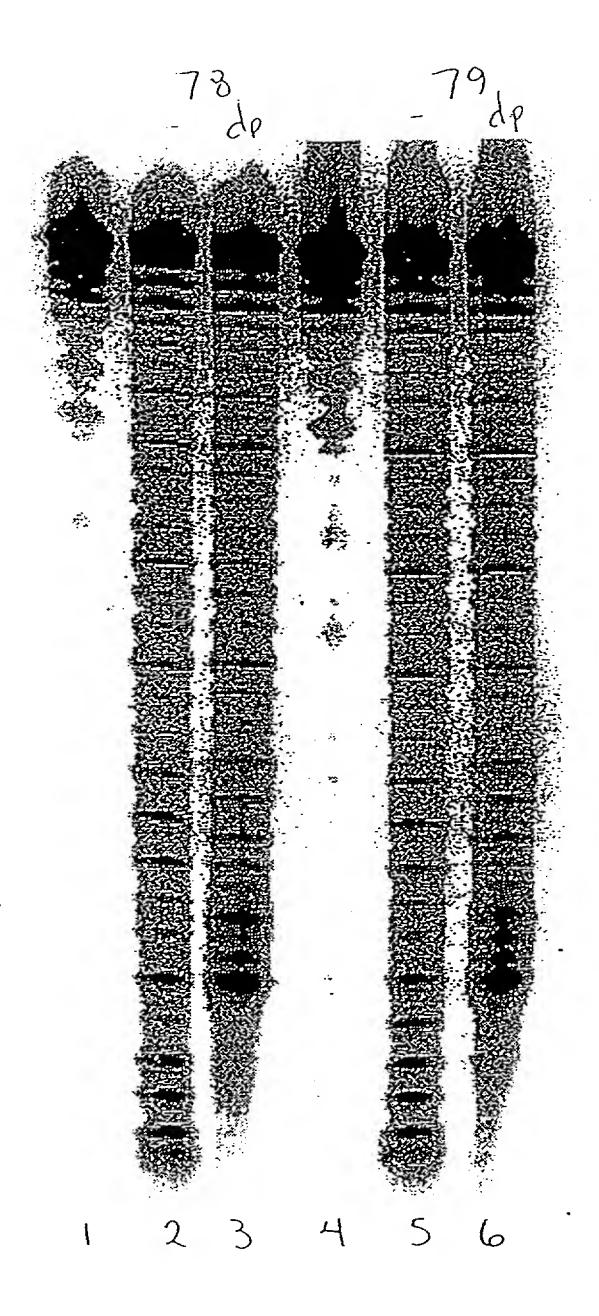












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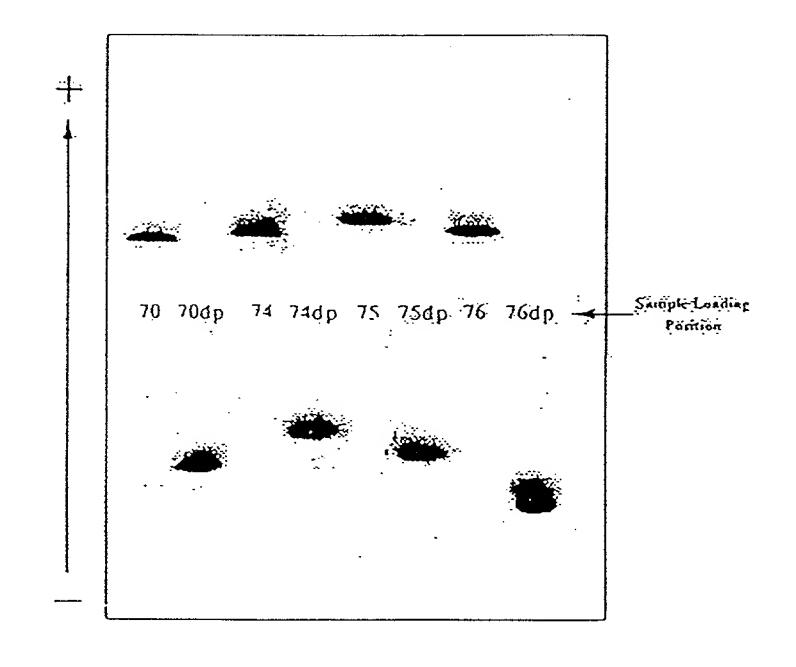
56

IZ \ ZI 0 70 (C10 aminoT's) 74 (C6 amino T's)

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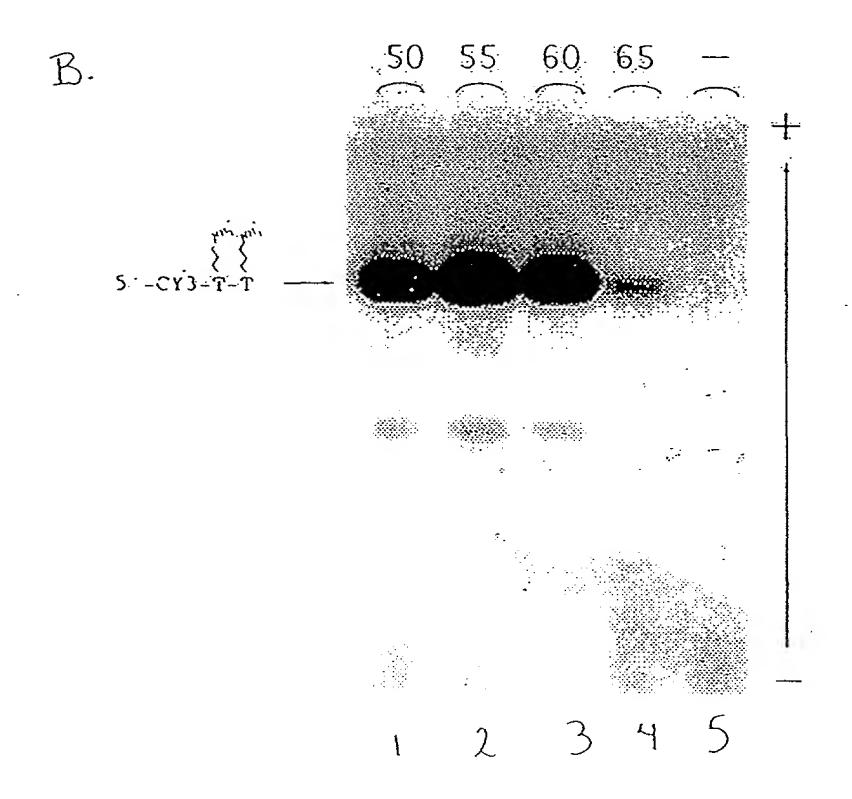
69/127





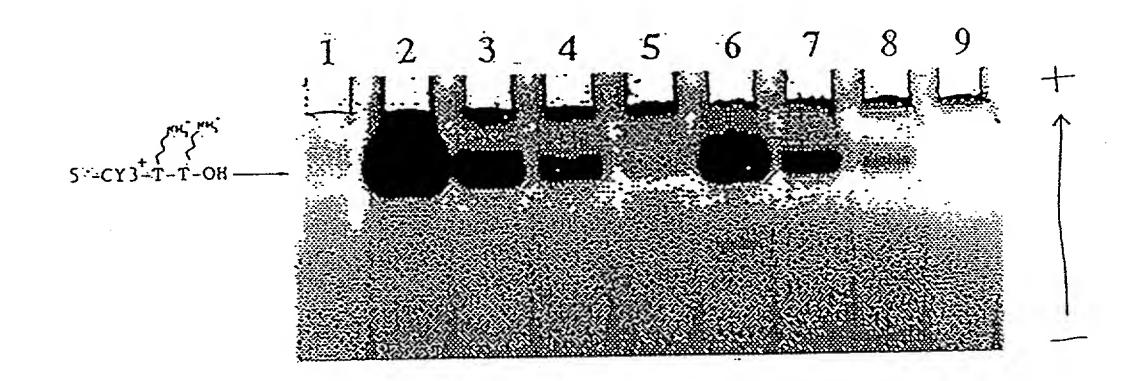
Cleavage Site

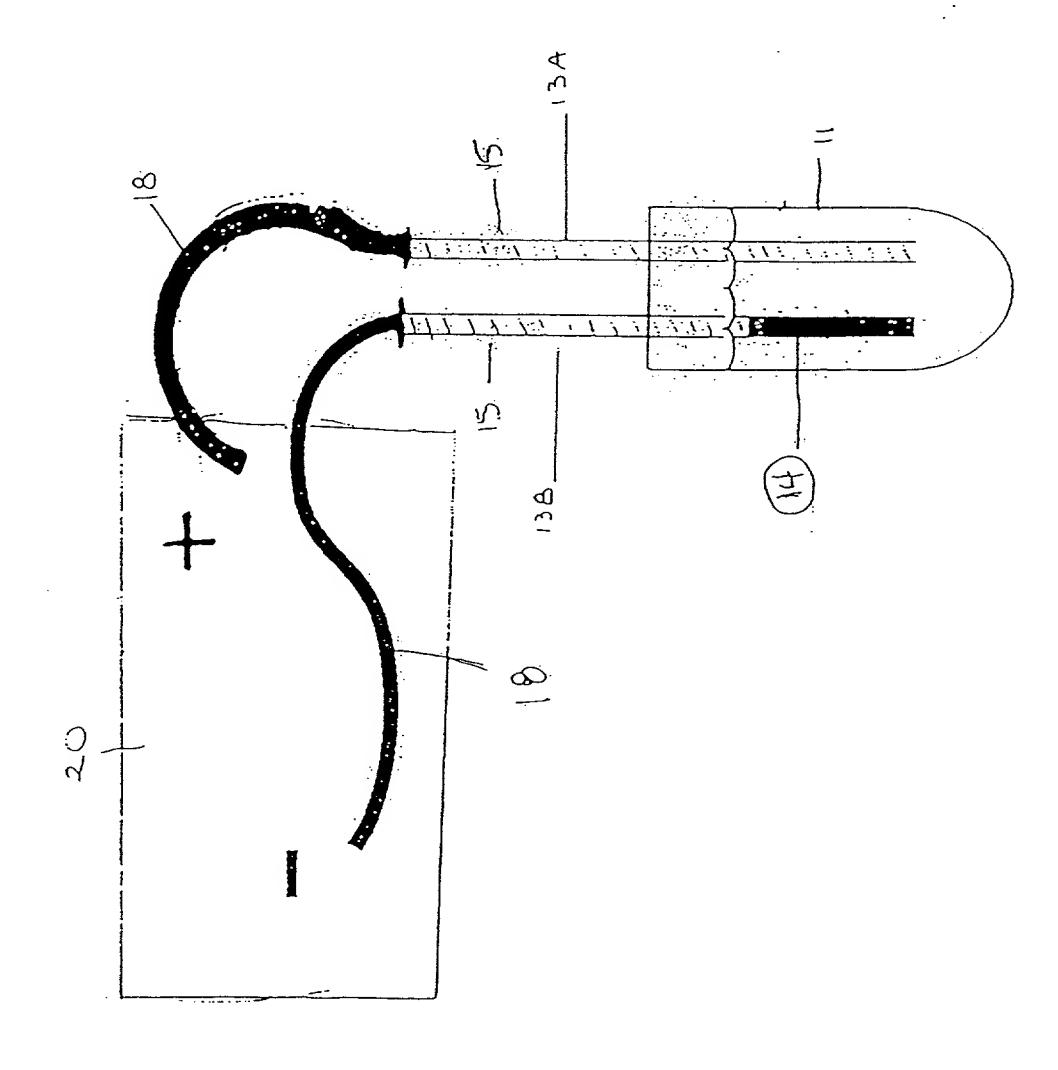
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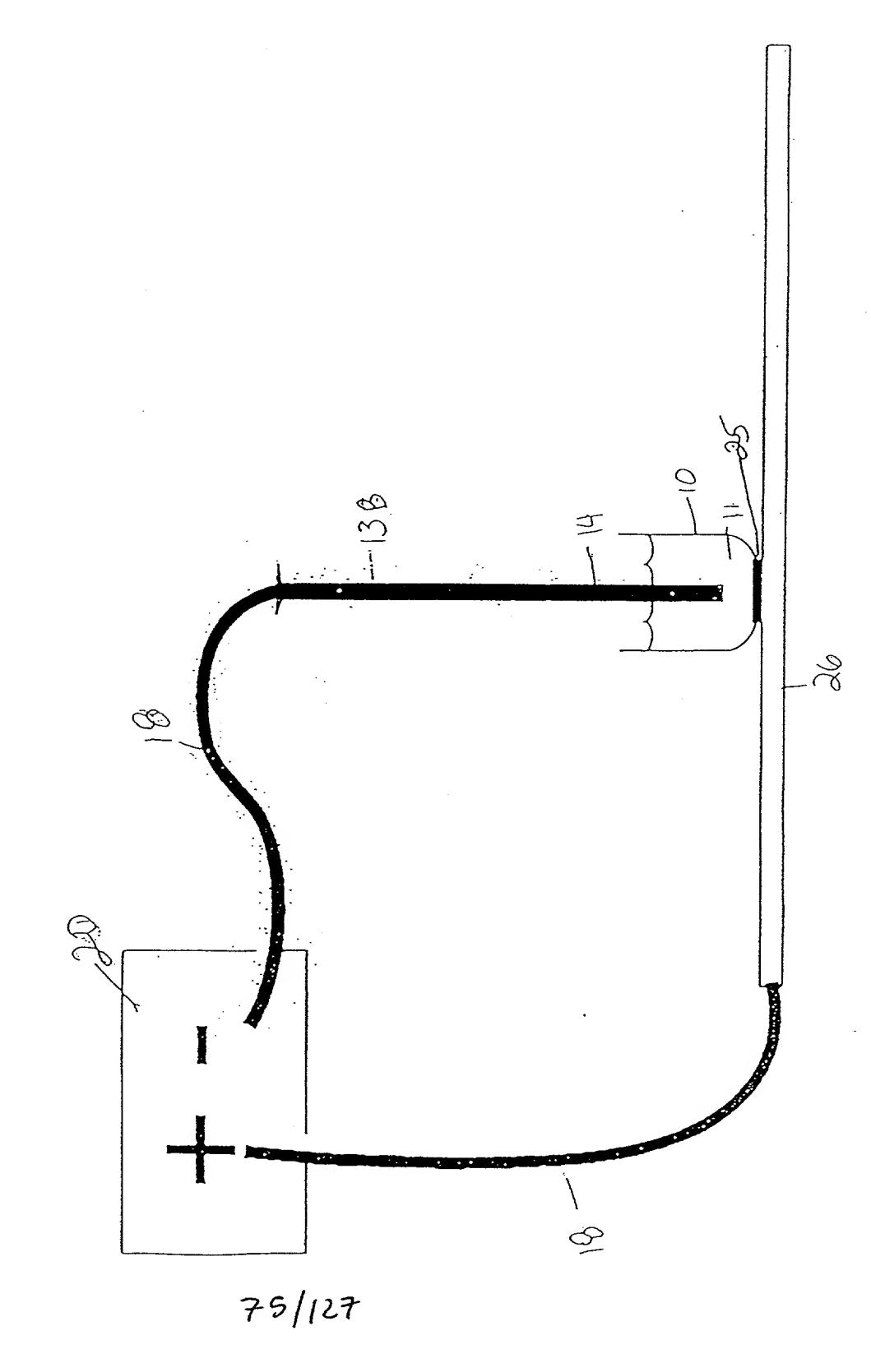


FIGURE 63





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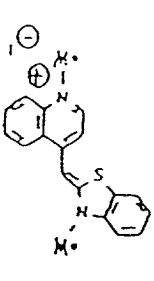
ر ج	Y AGAAAGGAAGGAAAGCGAAAGG	۲,	
3'	CGGCCGCTTGCACCGCTCTTTCCTTTCCCTTCTTTCGCTTTCC		
5 '	GCCGGCGAACGTGGCGAGAAAGGGAAGGGAAAGGGAAAGG	3'	
3'	CGGCCGCTTGCACCGCTCTTTCCTTCCCTTCTTTCCC		
·			
5'	AAGGAAGGAAAAGCGAAAGG		
J	CGGCCGCTTGCACCGCTCTTTCCTTCCCTTCTTTCGCTTTCC CAGAGGGAGGGAA	5.	b
5' 3'	GCCGGCGAACGTGGCGAGAAAGGAAGGGAAGAAAGGGAAAGG CGGCCGCTTGCACCGCTCTTTCCTTCCCTTC		
		J	
. .	CAGGGGAAGAAGCCAAAGC		
5 ' 3 '	GGAAGGGAAGAAAGCGAAAGG CGGCCGCTTCTTTCCCTTCCC	_	
	$C_{A_{G_{G_{G_{G_{G_{G_{G_{G_{G_{G_{G_{G_{G_$	J	C
5'	GCCGGCGAACGTGGCGAGAAAGGAAAGGGAAAGGAAAGG		
3'	CGGCCGCTTGCACCGCTCTTTCCTTTCCCTTTCTTTCCC	5 '	
	C_{AGC}		
5 '	·	3 '	
3'	CGGCCGCTTGCACCGCTCTTTCCTTCCCTTCTTTCGCTTTCC		
	$C_{A_{G_{G_{G_{J_{A_{C}}}}}}}$		d
5'	GCCGGCGAACGTGGCGAGAAAGGAAAGGGAAGGAAAGGGAAAGG		
3'	CGGCCGCTTGCACCGCTCTTTCCTTTCCCTTCTTTCGCTTTCC	5'	

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Ethidium Bromide

(1,3-propanediamino)propidium

(diethylenetriamino)propidium



Thiazole Orange

(N-N'-tetramethyl-1,2-ethanediamino)propyl thiazole orange (N-N'-tetramethyl-1,3-propanediamino)-propyl thiazole orange

EihO

TOED1

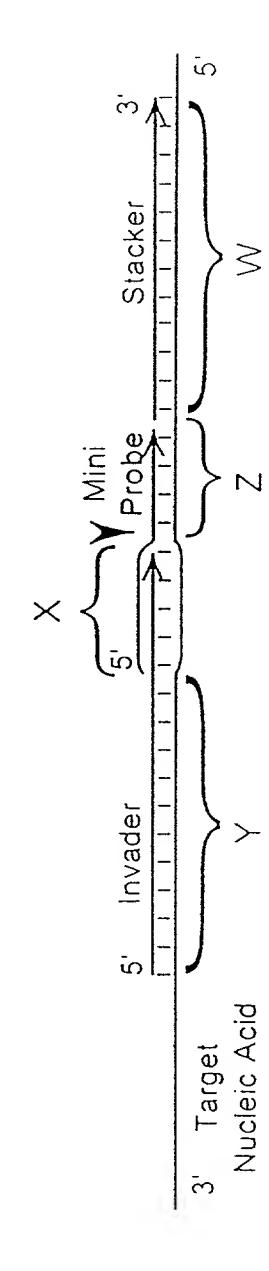
(R . H)

TOED2

(R = CH3)

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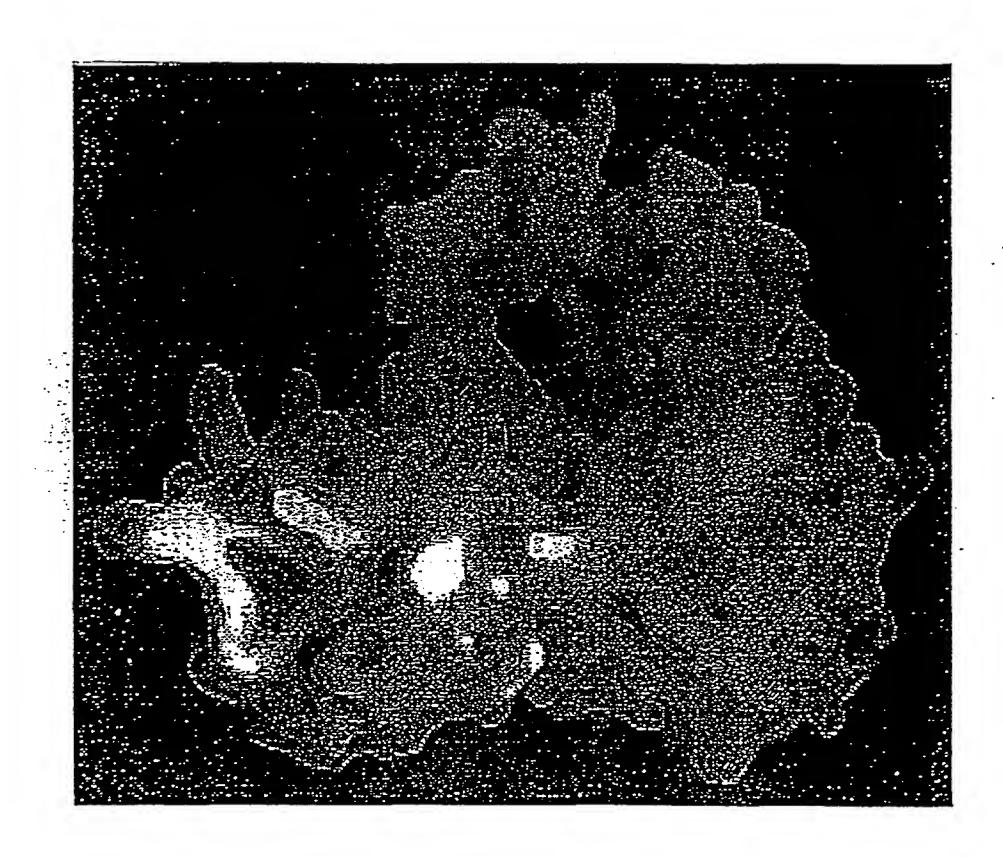


FIGURE 70-A

	<u>o</u> .	.0	30	0.	20	60	C
	GVOFGOFIPK	-NIISFEDLKG	KVAIDGMNAL	OFL ISIR	RDGSPLRNR	FITSAYNGVF	MUAFEN PR
	GVP IGE I IPR	-KEIELENLYG	KIAIDALNAI	OFLSTIR	KDGTPLMDS	RITSHLSGLF	PFUFEN! PR
	GIOGLAKLIADVAPS	IRENDIKSYFG	KVAIDASMSI	OFLIAVR	- GGDVLONE	ETTSHLMGMF	HUMFEN- PR
	GIHGLAKLIADV	IRENDIKSYFG	KVAIDASMSI	OFLIAVR	-GGDVLO	GETTS-LMGMFY	MUSFERIPR
	GIKGLNAIISEHVPS	IRKSDIKSFFG	KVAIDASMSL	OFLIAVR	ODGGOL TNE	ETTSHLMGMF	YST510 PRO
	GVHSFWDIAG P	ARPVRLESLED	RMAVDASIWI	OFLKAVR	OEGNAVKN-	SHITGFF	YSTRAD2.PR
	GVSGLWNILE P	KRPVKLETLVN	RLAIDASIWI	OFLKAVR	KEGNOLKS-	SHVVGFF	SPORAD13.P
87	GVOGLWKLLE C	GROVSPEALEG	ILAVDISIWL	OALKGVR	RHGNSIEN	PHLLTLF	HUMXPG PRO
2/	GVOGLWKLLEC	GHRVSPEALEG	VLAVDISIWL	OALKGVR	SHGNVIEN	AHLLTLF	MUSXPG_PRO
12	GVOGLWKLLE C	GRPINPGTLEG	ILAVDISIWL	OAVKGAR	ROGNAION	- AHLLTLF	XENXPG. PRO
7	/ /		TLSIDGHIWL	YESLKGCEA	HH001-	NSYLVTFF	CELRAD2 P
	80	06	100	0.1	120	0	0.
7	TIHLLENDITPIWVF	GEPPKLKEKTR	VRREMKEKAE	KMKEAIK	EOFEE	KYAKRVSYL	MJAFENI PR
す	TINLMEAGIKPVYVF	GEPPEFKKKEL	KRREAREEAE	KWREALE	日 日 日 日 1 1	KYAORATRVN	PFUFEN! PR
0	TIRMMENGIKPVYVF	GKPPOLKSGEL	KRSERRAEAE	OLOOAOA	GAEOE	KFIKRLVKVI	HUMPEN - PR
တ	TIRM-ENGIKPVYVF	GKPPOLKSGEL	KRSERRAEAE	OLOOAOE	GMEEE	X F T K R L V K V T	MUSPEN! PR
	TLRMIDNGIKPCYVF	GKPPOLKSHEL	KRSSRRVETE	KLA · · · E	3 1 3 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	KOERRL VK V S	YST510.PR0
	ICKLLYFGIRPVFVF	GGVPVLKRETI	ORKERROGKR	SAKSTAR	LLALOLONG	ONKROSOEVT	YSTRAD2 PR
	- CXLLFFG - XPVFVF	GGAPSLKROTI	KROARRLDRE	ZAT > LAZ	LLALOMRHO	LLKROADEVT	SPORADI3.P
 ,	LOXLLFFR-RP-FVF	GOAPLLXXOTL	X R R O R K O L A S			X TER LAATVI	
 .	しこメニード・スースアー・マドー・ファー・ロー・ロー・ロー・ロー・ロー・ロー・ロー・ロー・ロー・ロー・ロー・ロー・ロー	GUAPLLXXO-L	XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX	コンススーード	ـ لـ ـ لـ	OK-AASV-	SOUXTC TX
- <u>O</u>	RIORLLELKIIPIVVFO	NINASSSAHES	KOONEFVPRKR	RSFGDSPFT	N		CELRAD2 PR

FIGURE 70-B

2	
A C E C E C E C E C E C E C E C E C E C	O M D D D D D D D D D D D D D D D D D D D
Α Χ Χ Χ Χ Υ Υ Υ Χ Χ Χ Χ Υ Υ Υ Χ Χ Χ Υ	28 VAKDV KOPLAKF KY ESNNTKW GOFOKRK LSTGHAS HEAOKNP HEAOKNP SEAOKOK
V R N L L L A SE V R N L L L A SE V R N M F L A SE V R N M F N R N V R N F N F N R N V R N F N R N V R N F N R N V R N F N R N V R N F N R N V R N F N R N V R N F N R N V R N F N R N V R N F N R N V R N F N R N V R N F N R N V R N F N R N V R N F N R N V R N F N R N V R N F N R N V R N F N R N V R N F N R N V R N R N R N	270 AYELVRSG AVELVRSG - VRRLOPN - VRRLOPN - VRRLOPN - VRRVFOR - LKFSEWW - VKFKEWW - VKFKEWW - VKFKEWW
YDALLYGAPRV YDALLYGAPRV YDSLLFGAPRL MDCLTFGSPVLI MDTLCYRTPFLI SDVFLFGGTRV SDVFLFGGTRV SD I WLFGARHV SD I WLFGARHV SD I WLFGARHV	260 KGIGFKR/ KGIGLKK/ KGIGLKK/ KGIGLKK/ KGIGLKK/ KGIGLKK/ KGIGLKK/ KGIGLKK/ KGIGKK/ KG
180 60 V W A V V S O D 65 V Y A A A T E D 6K V Y A A A T E D 7 V D G 1 V T D D 8 V V S G T 1 T D D 8 V V S G T 1 T D D 8 V V S G T 1 T D D	250 MGTDYNPGGV VGTDYNPGGI GIGPKRAVDL GIGAKRAVDL GIGAKRAVDL TVGPVTALKL TVGPVLALEI TVGCVTAMEI TVGCVTAMEI
170 E A O A S Y M A K K E A S C A A L A K A E A S C A A L A K K E A O C A E L L O L E A O C A I L D L T E A O C A I L D L T E A O C A I L D L T E A O C A I L D L T E A O C A I L D L T E A O C A I L D L T E A O C A I L D L T E A O C A I L D L T E A O C A R L E D L	240 LODL I D I A I F LGSDYCES I R LGSDYCES I R LGSDYTEG I P LGSDYTEG I P LGSDYTEG I P LGSDYTEG I P LGSDYTEG I P
000 000	230 VLEDLRIS VLKELKLT OF VDLC IL OF VDLC IL OF VDLC IN NM I EL AOL VL I NL A YL XL I NL A YL XL I NL A YL
MANENCKYLLSLMGIP OHNDECKHLLSLMGIP OHNDECKHLLSLMGIP OHNDECKHLLSLMGIP OHNDECKHLLSLMGIP OHNEEAOKLLGLMGIP OMFLESOELLRLFGIP OMFLESOELLRLFGIP OMFLESOELLOLFGIP OHVYKTNALLTELGIK	220 NVYVE-IKPEL I LEEV EFHLSRILOELGLNOEO EFHLSRILOELGLNOEO EFHLSRVLOELGLNOEO FYDAESILKLGLDRKN YYOYVDFHNOLGLDRNK YYOYVDFHNOLGLDRNK YYOYVDFYSOLGLDRNK YYOYVDFYSOLGLDRNK YYOYVDFYSOLGLDRNK
000 9 7 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	127

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FIGURE 70-C

10)) j	300	0 8	320	330	340 36	50
2000 2000 2000 2000 2000 2000 2000 200	CKKEVEYYDE IKRI OKOSOVOLYA IKEF PVPENWLHKEAHOL KIPENWLHKEAHOL KIPENWPYKOARML KIRPNPHOTKVKKK KYAENPYOTKVKKK KYAENPYOTKVKKK KYAENPYOTKVKKK KYAENPYOTKVKKK	FKEPKV FLEPEV FLEPEV FLEPEV LVGK-IILDDDF LVGK-IILDDDF LRKLOLTPGF LRKLOLTPGF LRKLOLGCOV	FPSVMVYDAYL FPNPAVAEAYL FPNPAVAEAYL FPNPAVAEAYL FPNPAVASAYL	TONY TONY LOPESVE 	SLSLKLPDKEG NLVWRDPDEEG ELKWSEPNEEG YLKWSPPKEKE NLKWSPPKEKE SFLWGVPDLDY SFLWGKPDLDX SFLWGKPDLDX SFLWGKPDLDX SFLWGKPDLDX SFLWGKPDLDX	FLVDENDFNY FLCDEHDFSE FMCGEKOFSE YLCDDKKFSE FLMATOLGWPH FCORYFGWNR FCORYFGWNR FCORYFGWNR FCORYFGWNR	E PFUFENI PRO E YSTS10 PRO E YSTRAD2 PRO T HUMXPG PRO E XENXPG PRO E CELRAD2 PRO
84/12	360	370	380	390	400	4.10	O F CI
300 300 300 300 300 300 400 400 400 400	A O O O O O O X O X O X O X O X O X O X	GS-TOGRLDDFF GS-TOGRLDDFF SG-TOGRLDDFF KKK AOOTOLRIDSFF LRRKKYNFPVGF	FKVT	AKRIKSORLN AKLIKSARLS 	X X X Y Y Y Y Y Y Y Y Y Y Y Y Y Y Y Y Y		- MJAFENI PRO - HUMFENI PRO - YSTSIO PRO - YSTRAD2 PRO - YSTRAD2 PRO - YSTRAD13 PRO - YSTRAD13 PRO - YSTRAD2 PRO -

The street of th

FIGURE 70-D

490 MJAFENI PFUFENI -GSLS HUMFENI	GSL 	SGO NKTKOKTL MJAFEN P KAKTGAAG HUMFEN P KAKTGAAG HUMFEN P KAKTGAAG HUMFEN P KK YSTRAD2 P RKLRRARG HUMXPG PR TKSKTMKE XENXPG PR TKSKTMKE XENXPG PR
7180	ADAFGESKGS SESSOGSSSE SESPOESSCE TLSSKAYSSO CESLEDYISA	550
470	PMSEE OAD GGFLGETCL GGFLGETCL GGFLGETCL KNFTPIVEP	540 540
7 60	SFKNO SNOS LSDSKRKNTC VPKRRRPSGN VPKRRRPSGN FCSOEDODPG IPDFFAATKS	530 530 530 530 530 530 530 530 530 530
450	KSKRLENALS EESSSLKRKR KETS -OGTKRRKPT HLTTTVAOTR	520
1 1 1		510 510 510 510 510 510 510 510 510 510
430	6 SNLTOFFEGGNTN 6 EKEFELLDKAKRK 7 KRECTNORKGOKT 8 ERECTNORKGOKT 9 MKECGWPATRTOK	500 2 SAKRKEPEPKGST 3 SAKRKEPEPKGST 4 KEOLAAAKRAOE 4 KEOLAAAKRAOE 6 NVORRTAAKEPKT 9 SARORSAAESSKI 9 SARORSAAESSKI

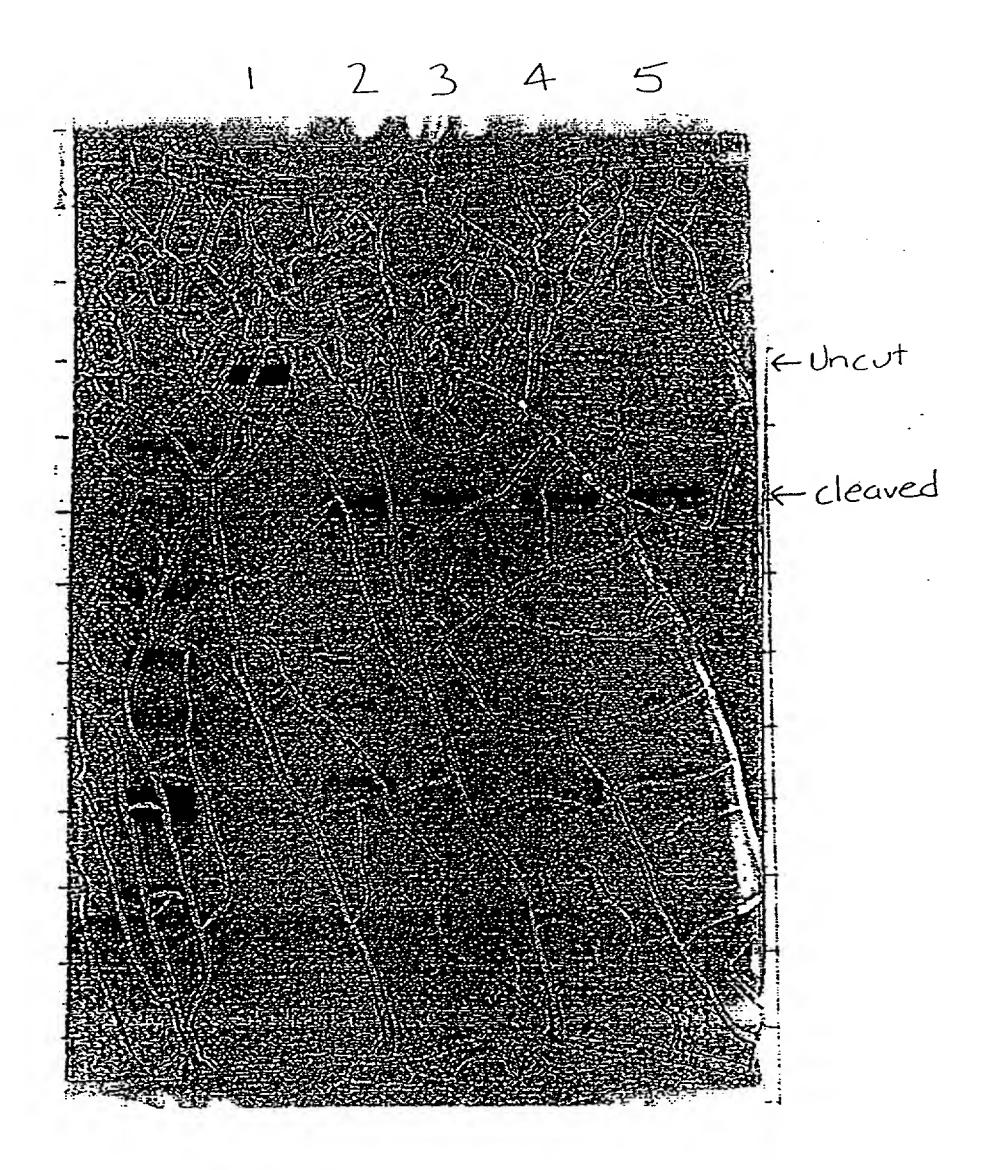
322 DAWFKZ 335 ESWFKR 375 KFKRGK 373 KFRRGK 377 VTKGRR 183 SKRRRK 546 RKRKTZ 538 RKKKKT 523 TVKRK 129 ELGDSD

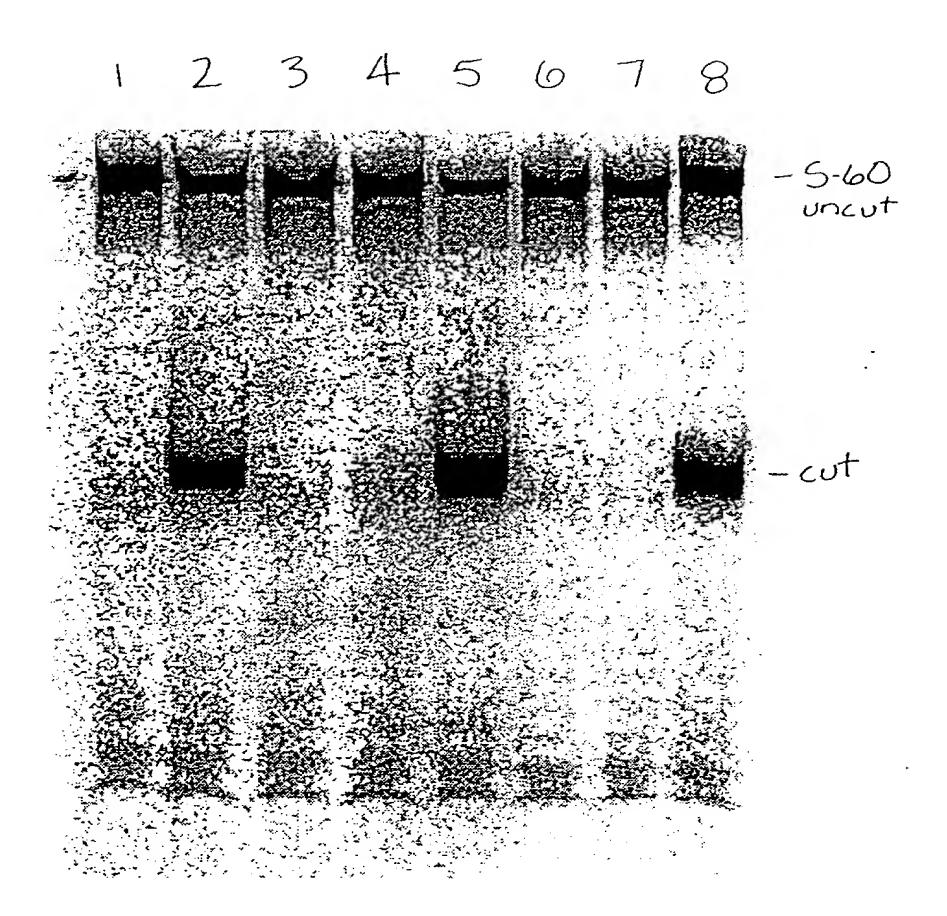
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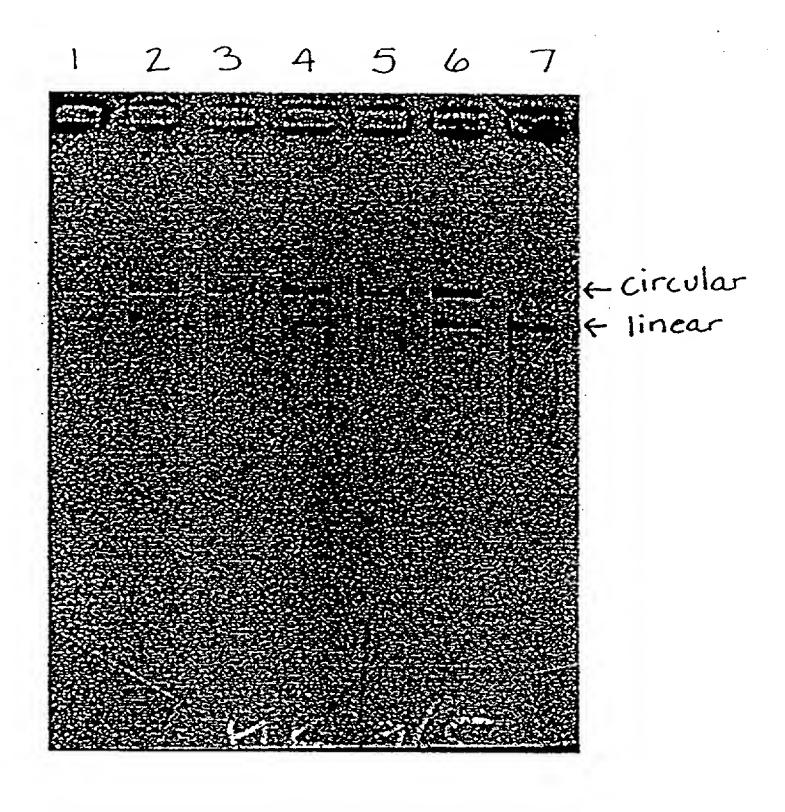
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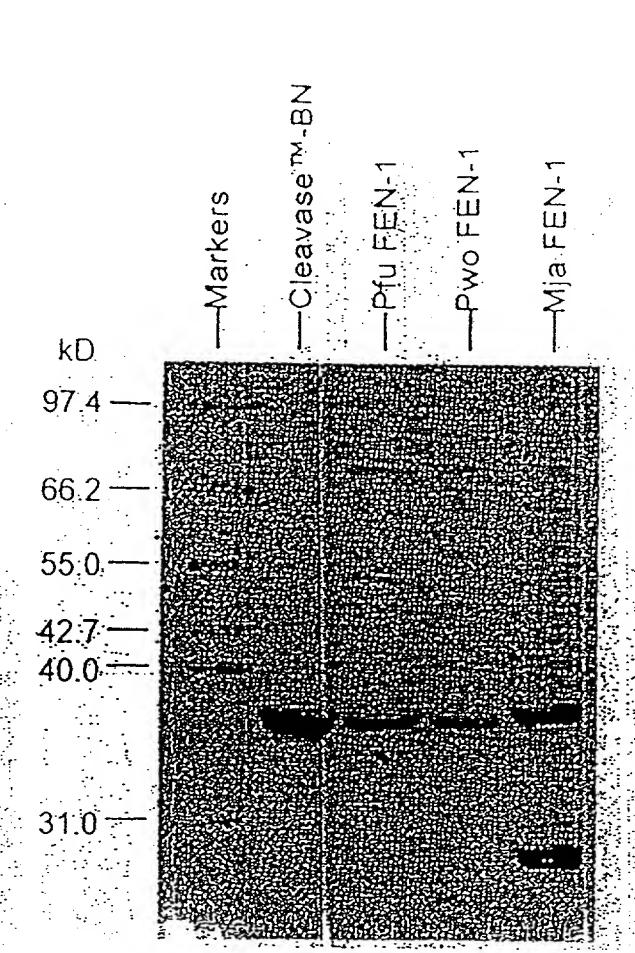
MUNAPC YSHEN YSHEN YSHEN YSHEN YSHEN YNAPC CELRPC

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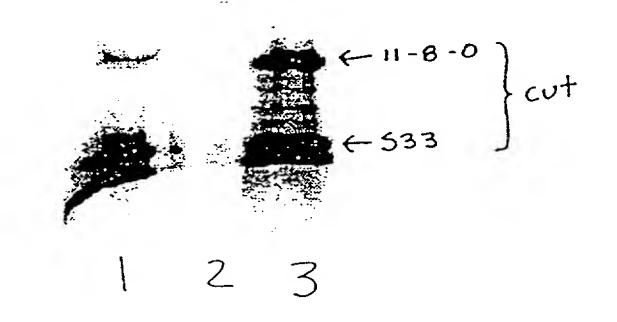


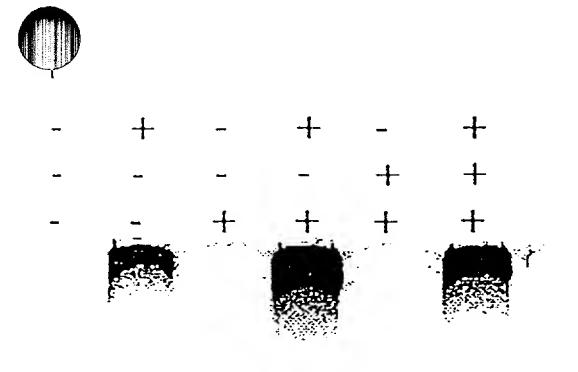
Enzyme Cleavase - Mja

BN

Enzyme Cleavase - Mja

Enzyme (11-8-0) uncut

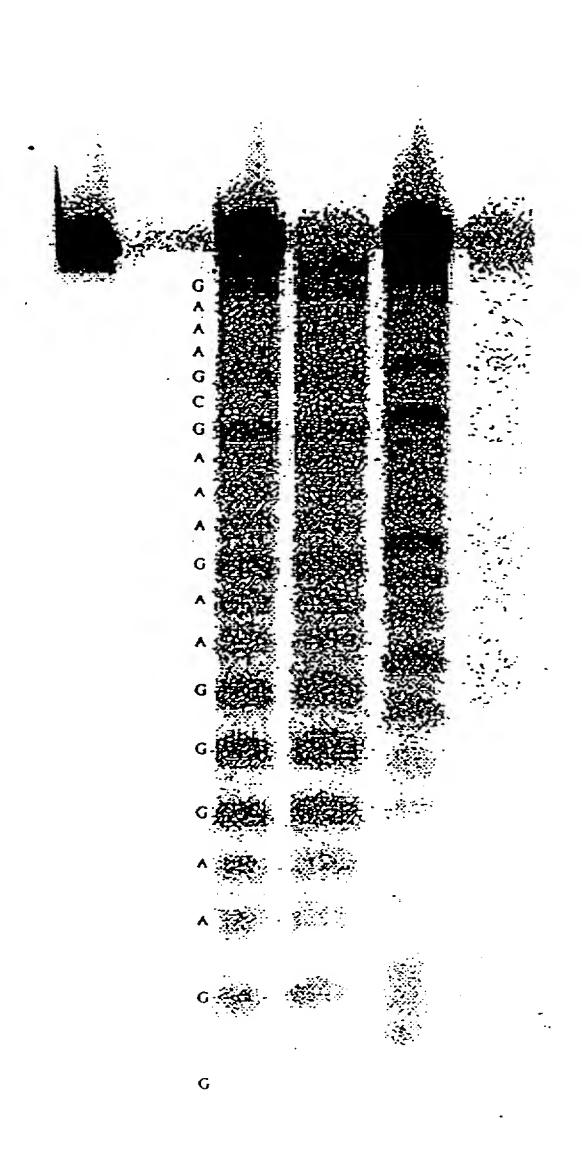




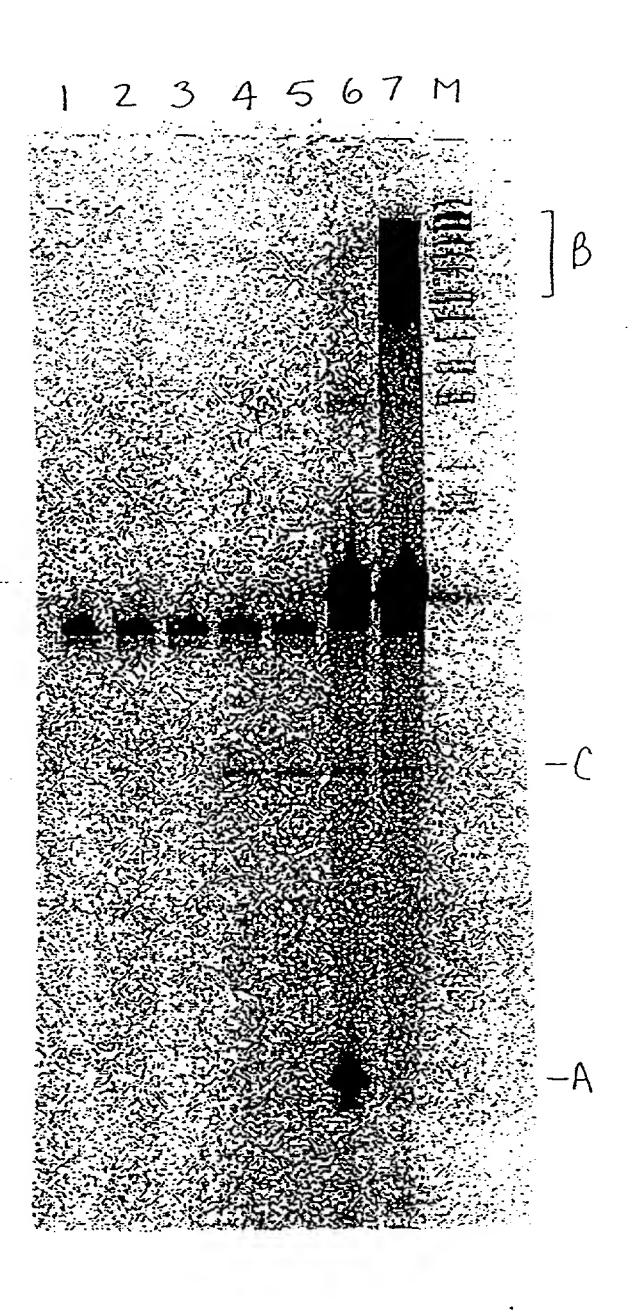
Terminal Transferase

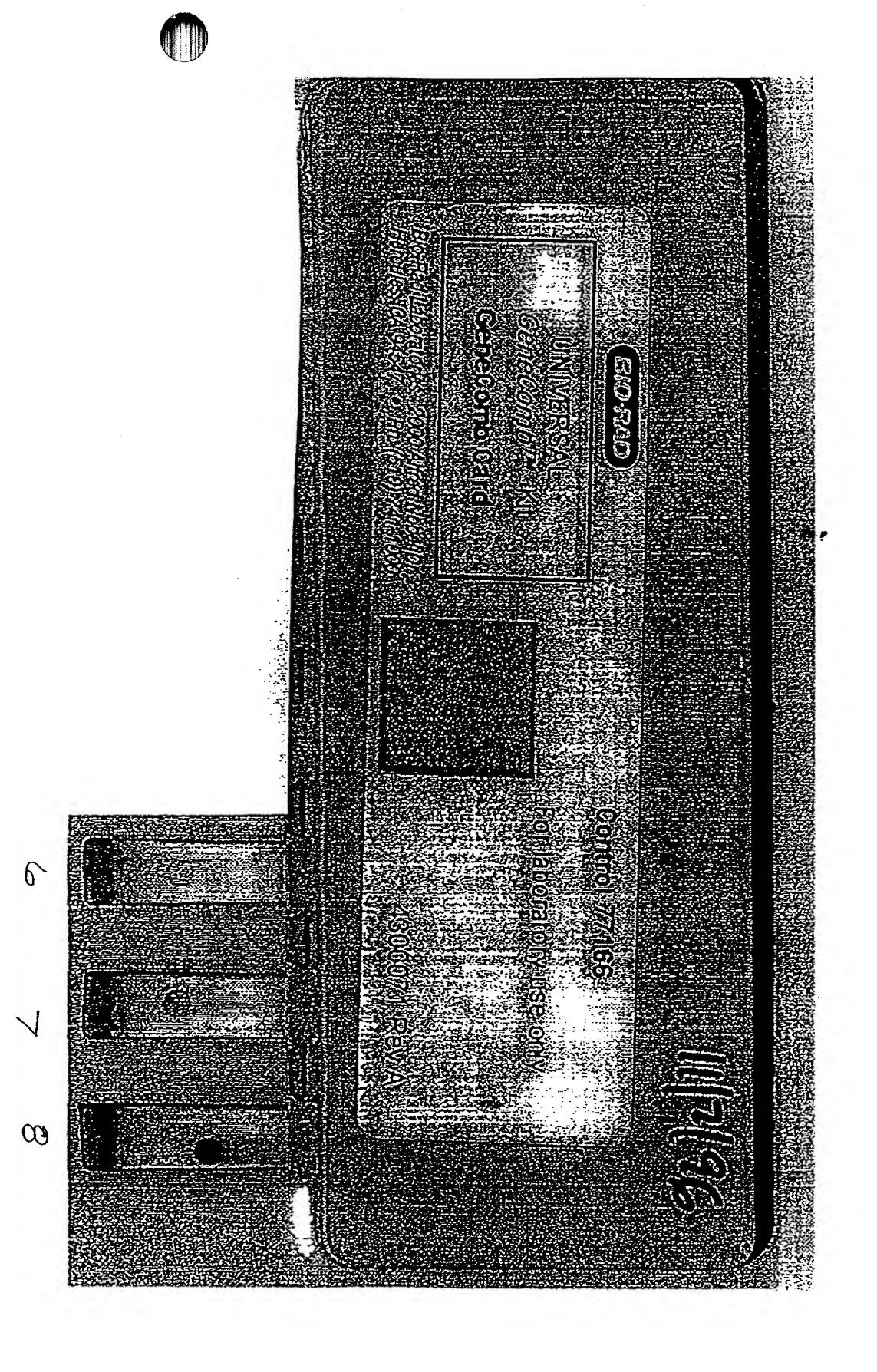
Alkaline Phosphatase

Thermal Degradation

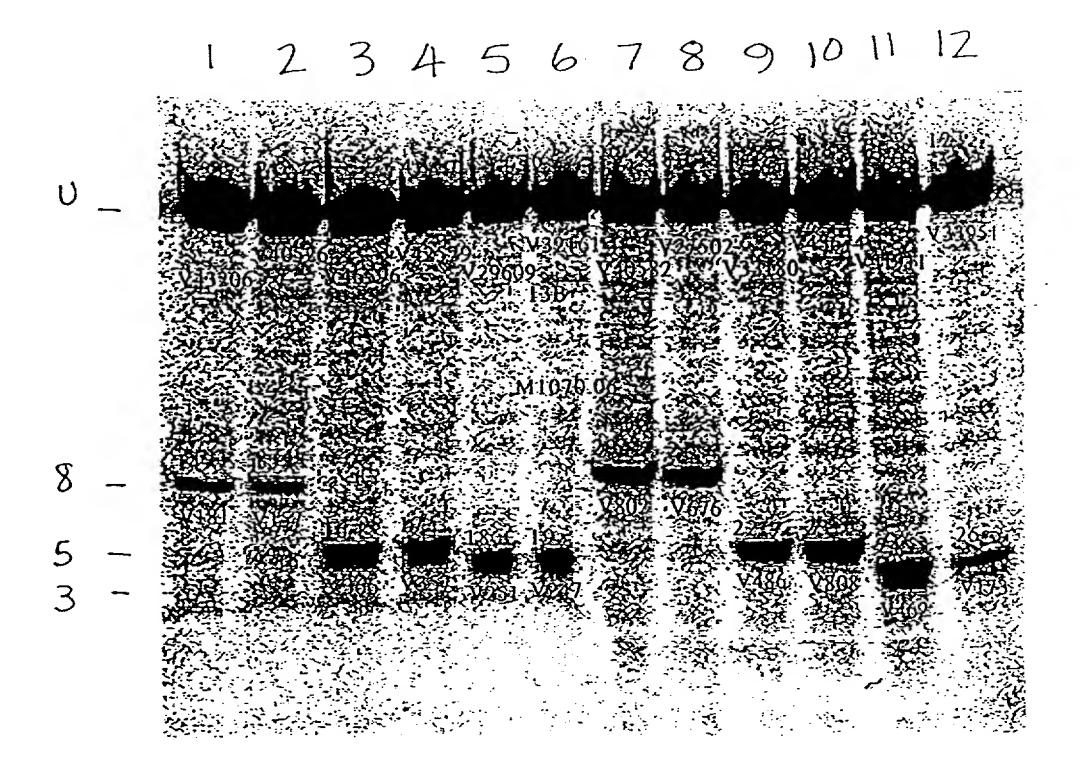


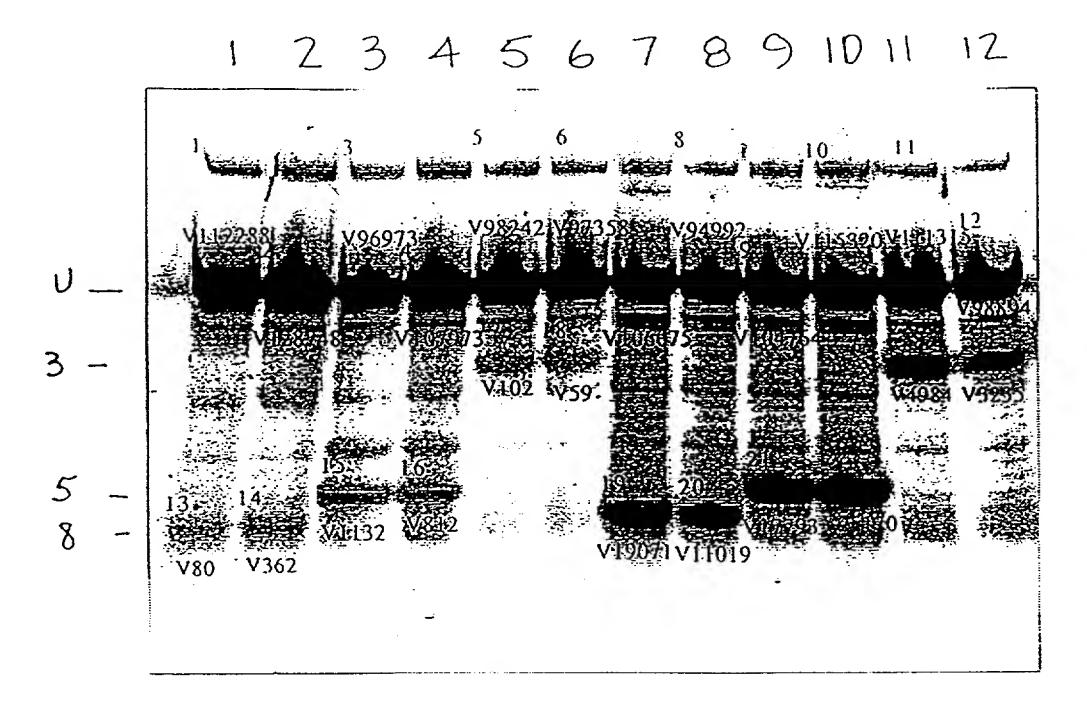
5'-nAGAAAggaaggga <u>ag</u>aaagcgaaagG-3'



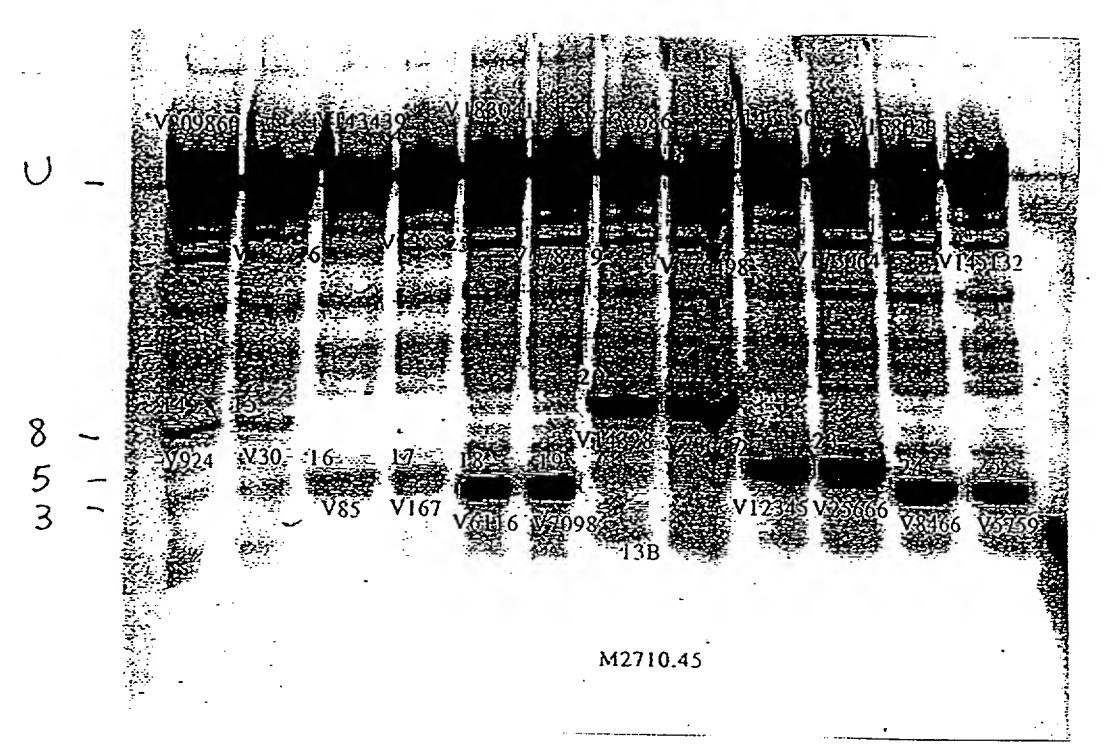


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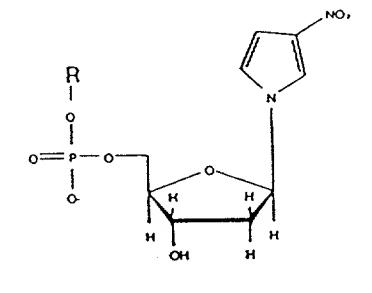




1 2 3 4 5 6 7 8 9 10 11 12



V4161 B



3-nitropyrrole

5-nitroindole

INVADER CTTTTCACCAGCGAGACGGG-3'-61
109-3-ATAACCCGCGGTCCCACCAAAAAGAAAAGTGGTCGCTCTGCCC-5'
09876543210987654321
123456789

TATTGGGCGCCAGGGTGGTTTTT TATTGGGCGXCAMGGXGGTTTTT

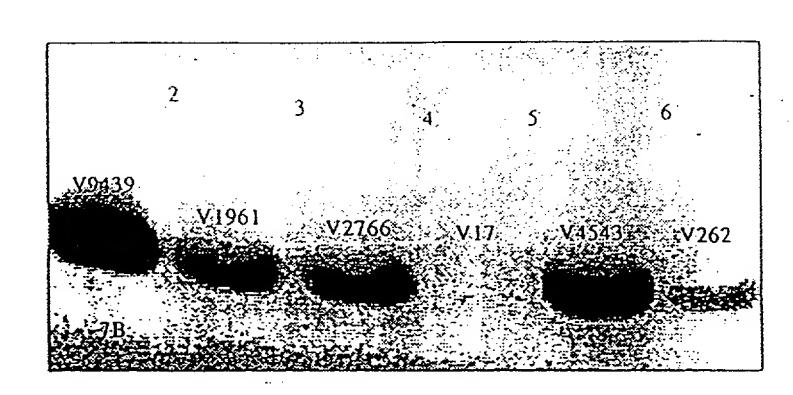
X = 5-nitoindole or 3-nitropyrole
M = mutation site

18ase Allcorp 18ace Allcorp Mismoth 2 NI mismoth 1 NP 2 NI

Pismatch INP

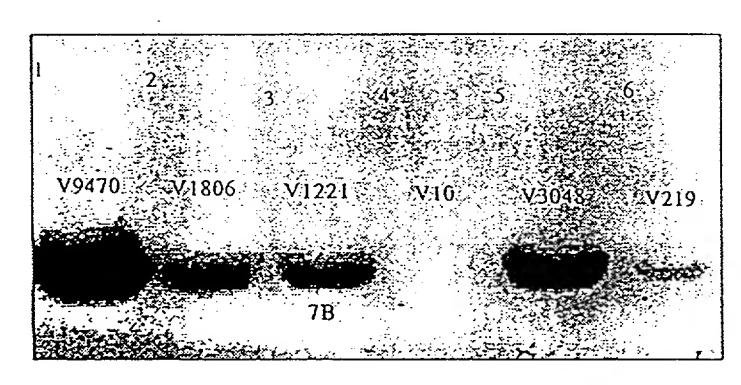
Inual 4 67 114 115 116 112 113

52°C



Hard had not deal that the first the two lines had then it had the first that the first that the first that

55°C



58°C



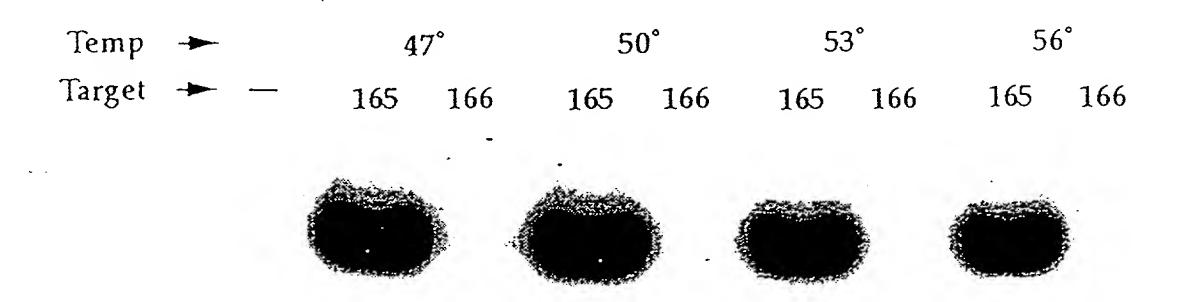
Codon 13
Point Mutation

166 (wt)
3'-CAGTTCCGTGAGAACGGATGCGGTGGTCGAGGTTGATGGTGTTCAAATATAAGTC.-5'

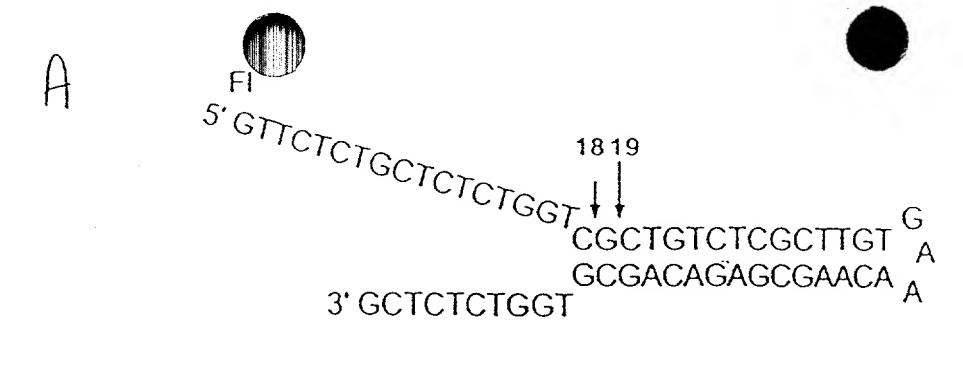
165 (mutant)
3'-CAGTTCCGTGAGAACGGATGCAGTGGTCGAGGTTGATGGTGTTCAAATATAAGTC-5'

5'CY3' CACCAG

3'-GCAGTTCCGTGAGAACGGATGCXGTGGTCGAGGTTGATGGTGTTCAAATATAAGTC-5'
162 GCTCAAGGCACTCTTGCCTACGA CTCCAACTACCACAAGTTTATATTCAG 164

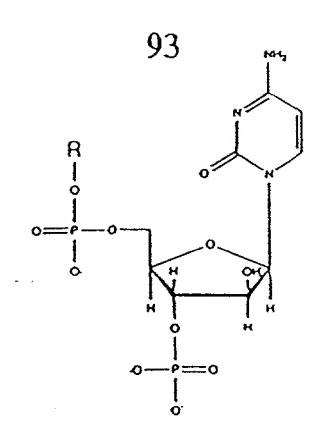


Harry House The Marie Ma



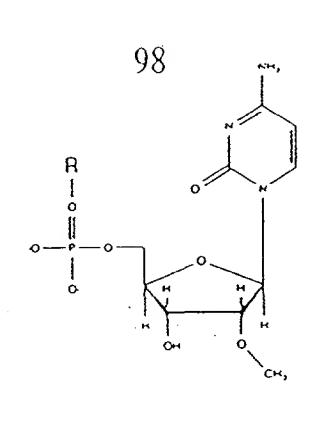
105/127

Mader 3'-end Substitents



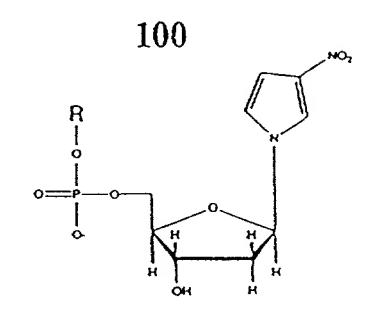
93dp

3'-Cytosine Arabinose



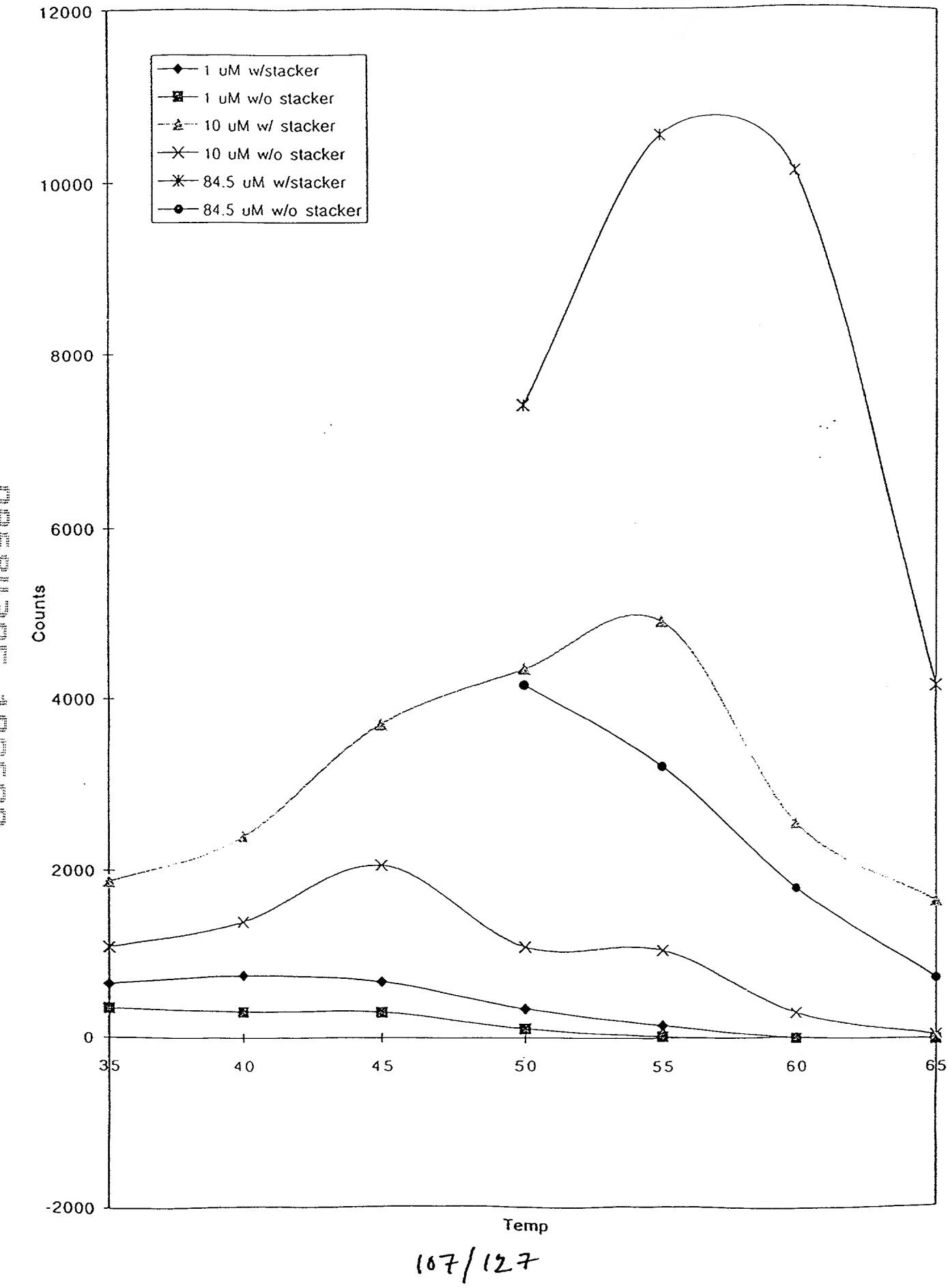
3'Phosphate C Arabinose

2'-Omethyl Cytosine



5-nitroindole

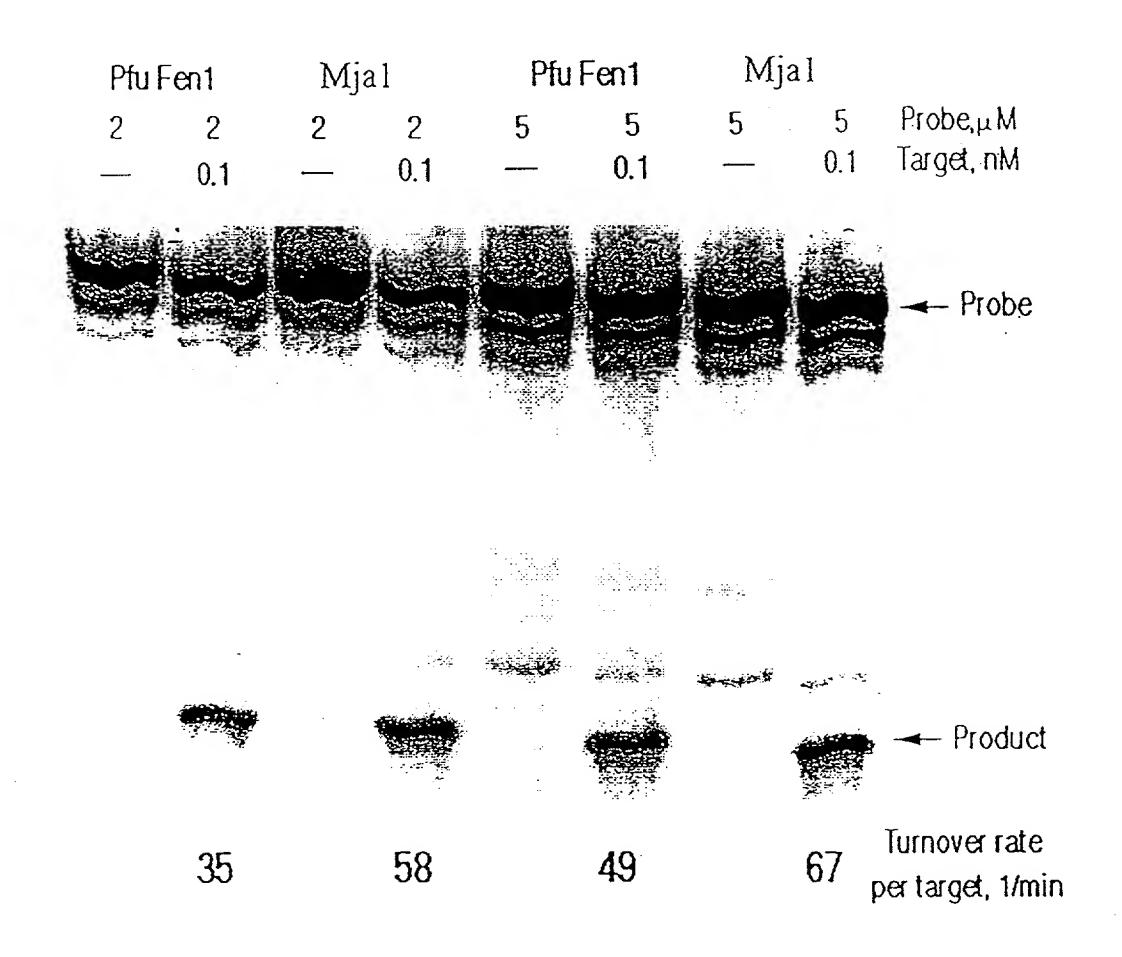
3'-deoxy-adenine

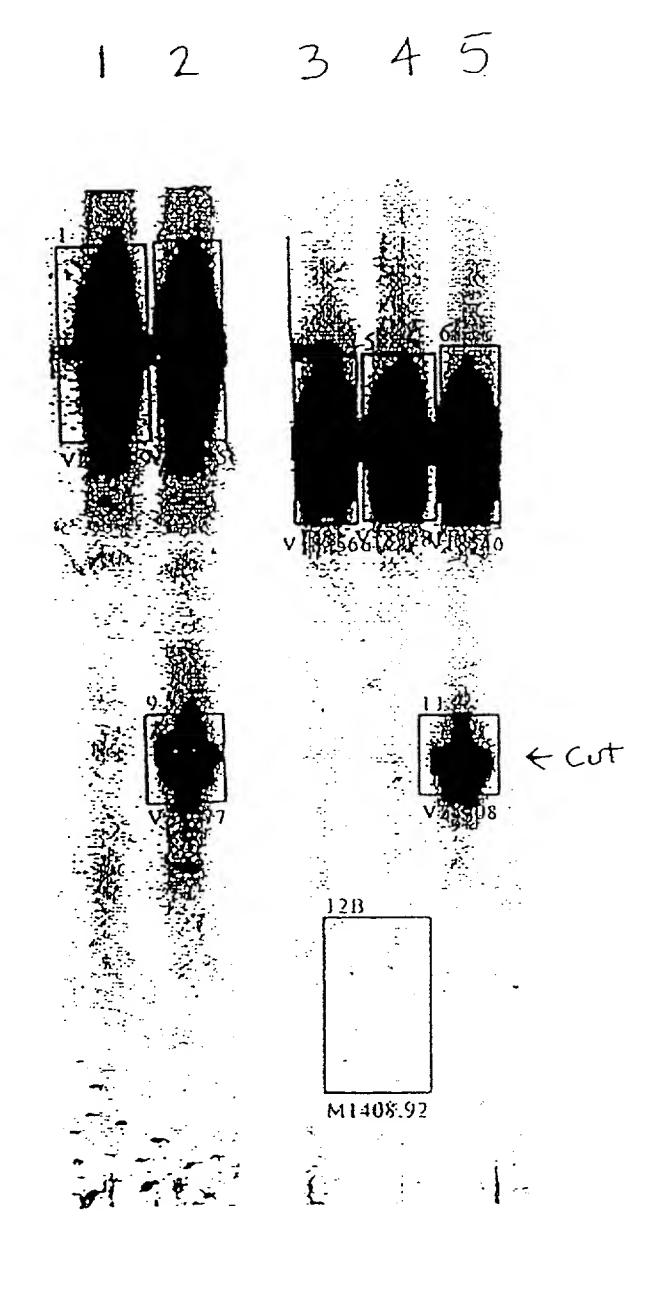


3 GTGCTCAGAGAAAGGAAAAGGT cleavage cleavage site site

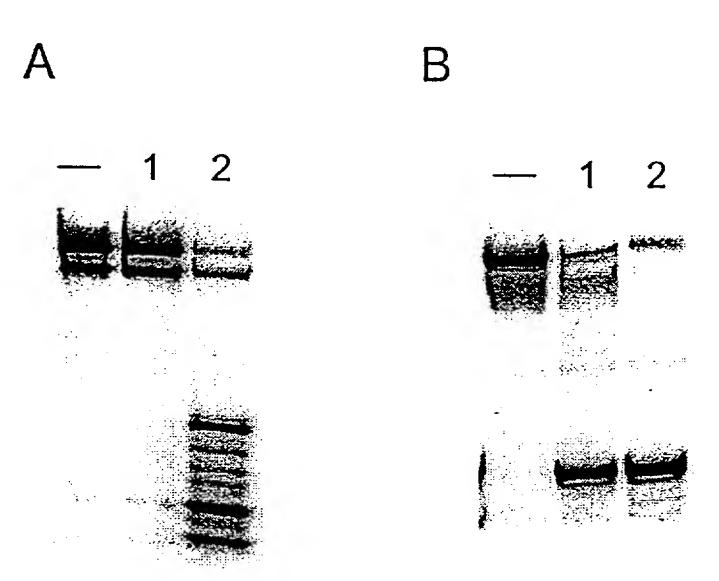
1 2 3 4







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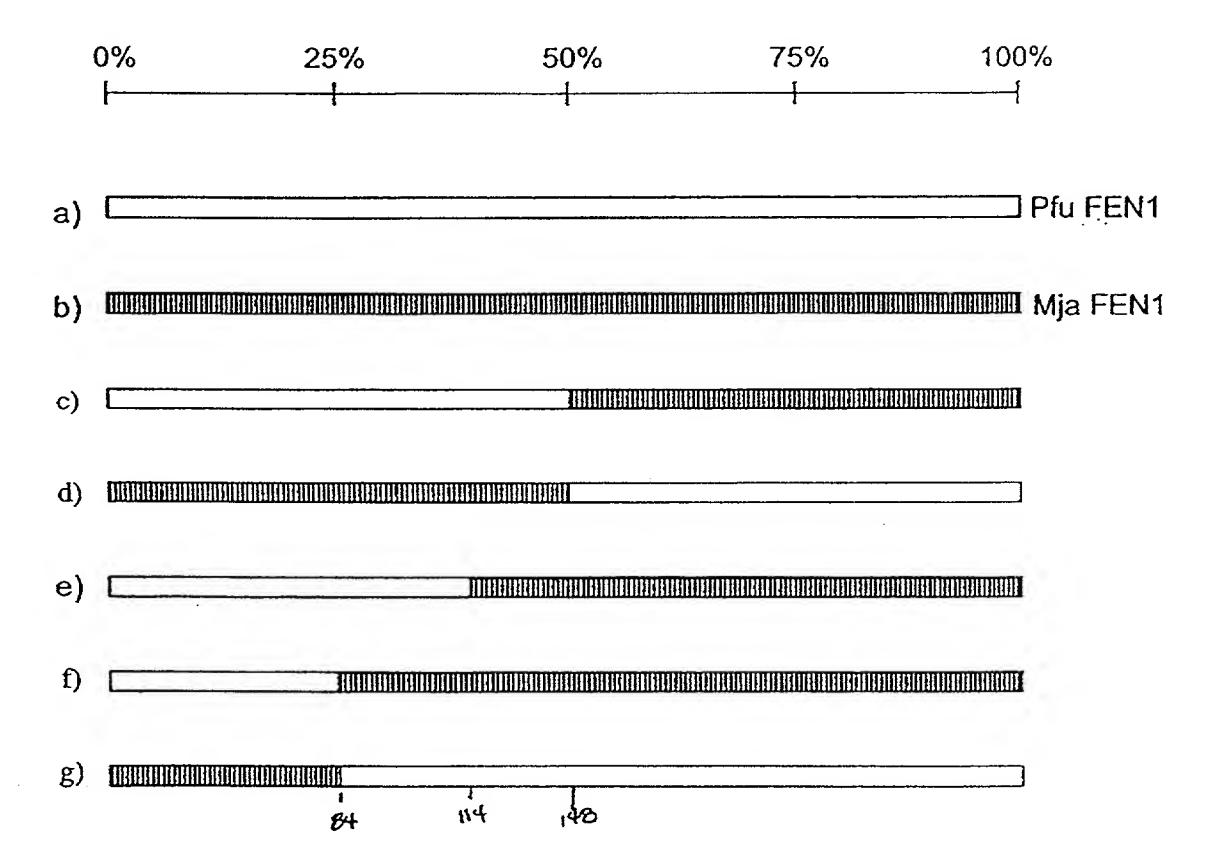


FIGURE 98A

— 1 2 97c 97d 97f 97g

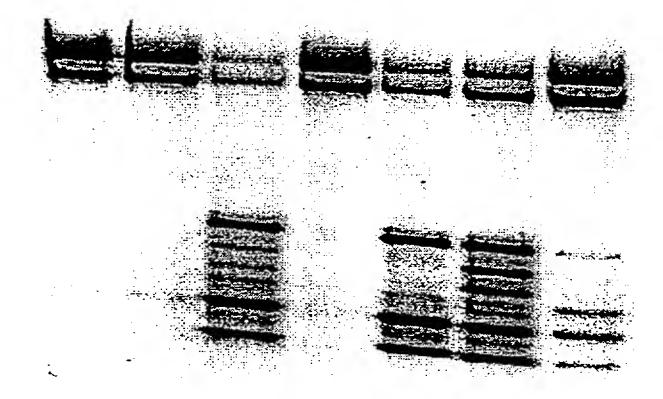
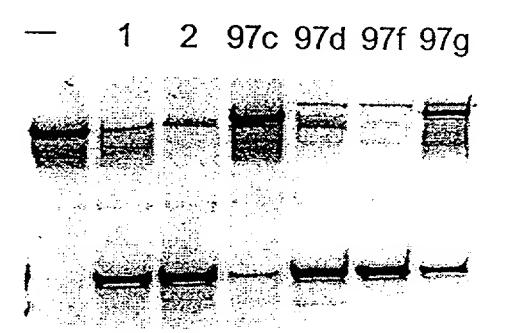
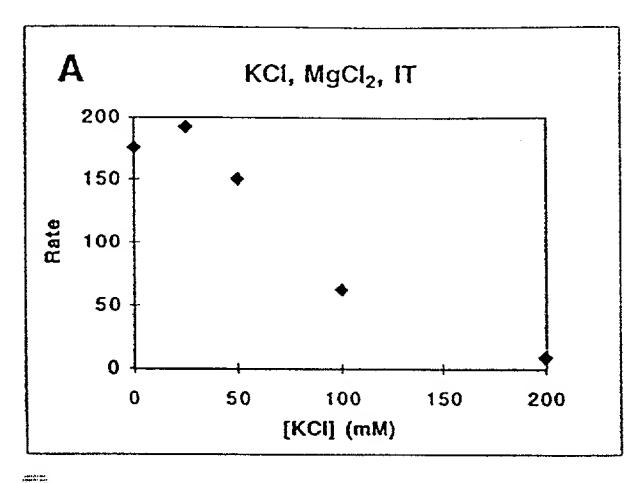
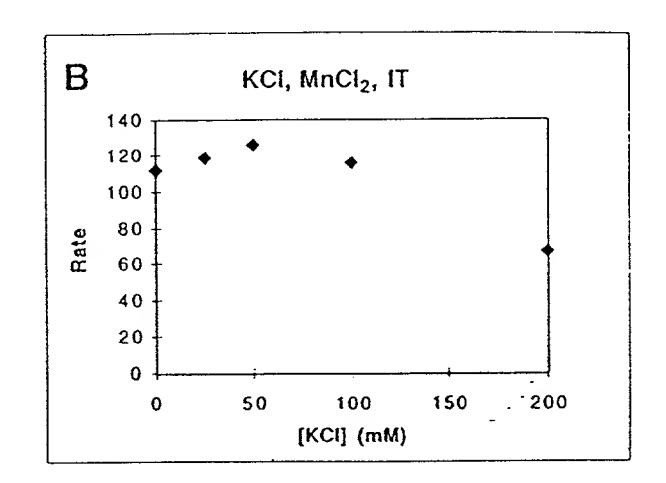


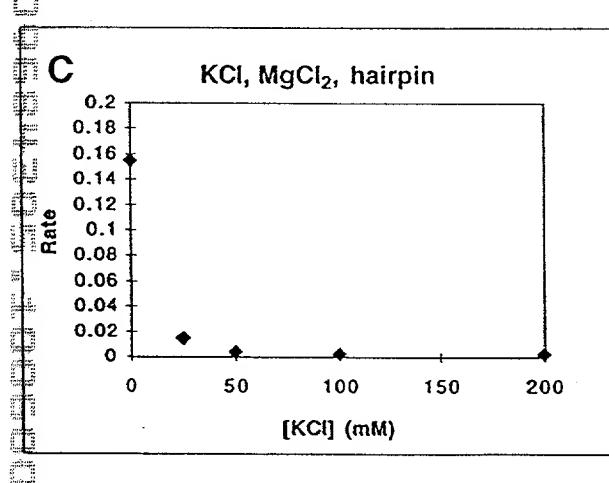
FIGURE 98B

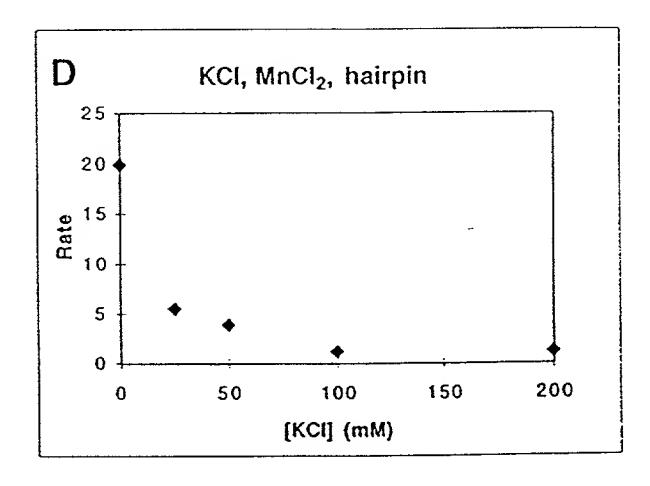


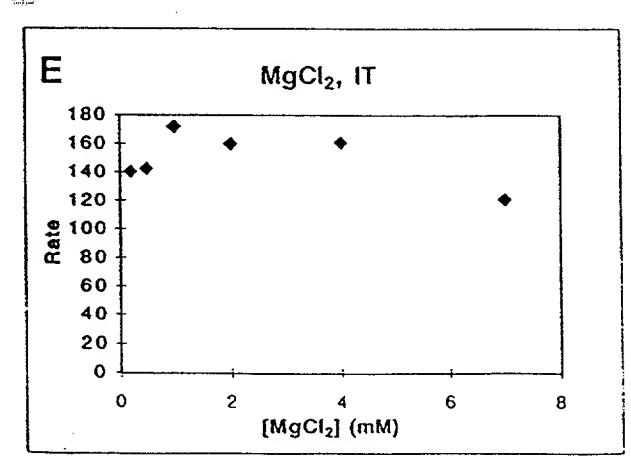












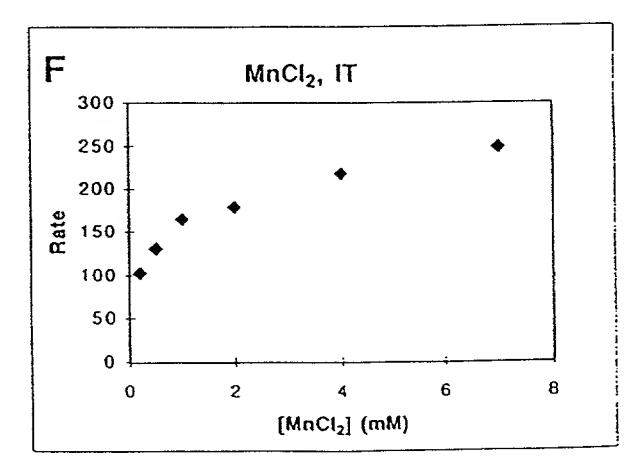
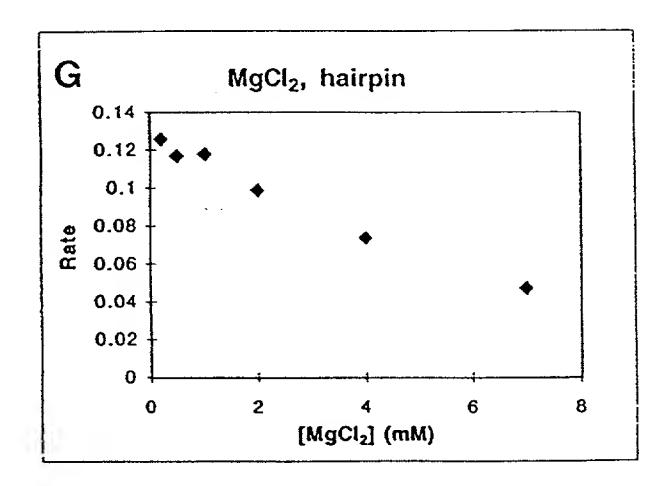
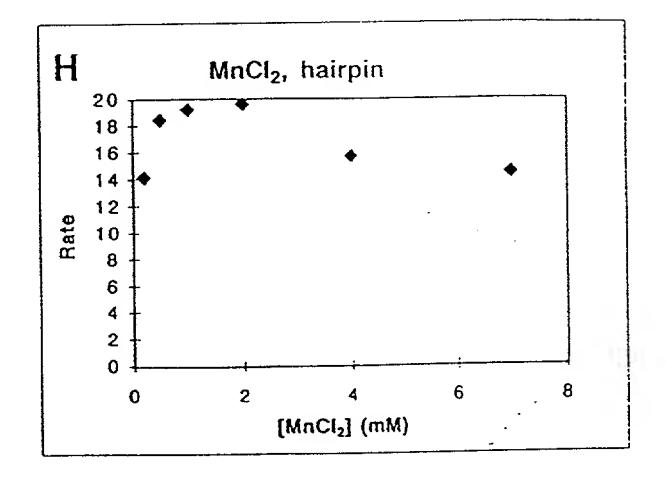
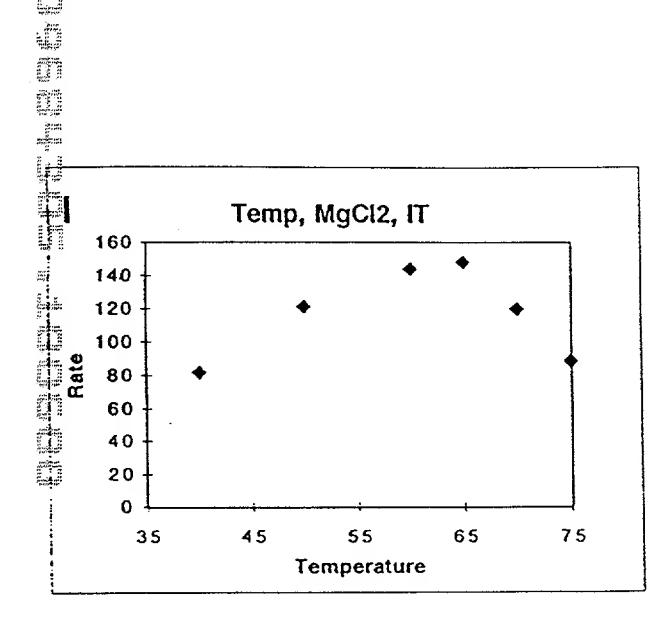
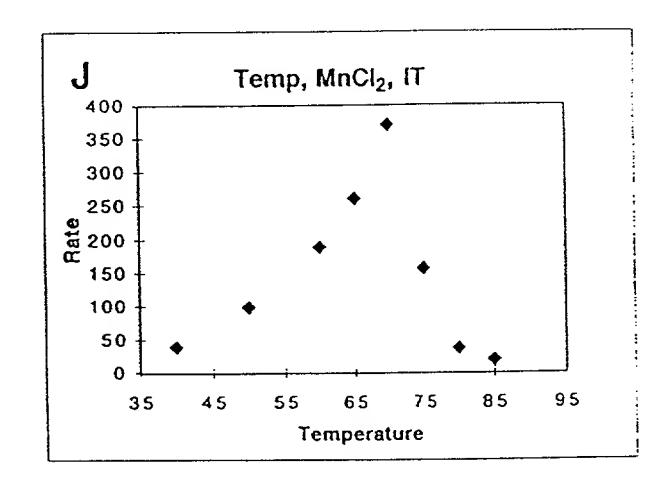


FIGURE 100 (cont.)









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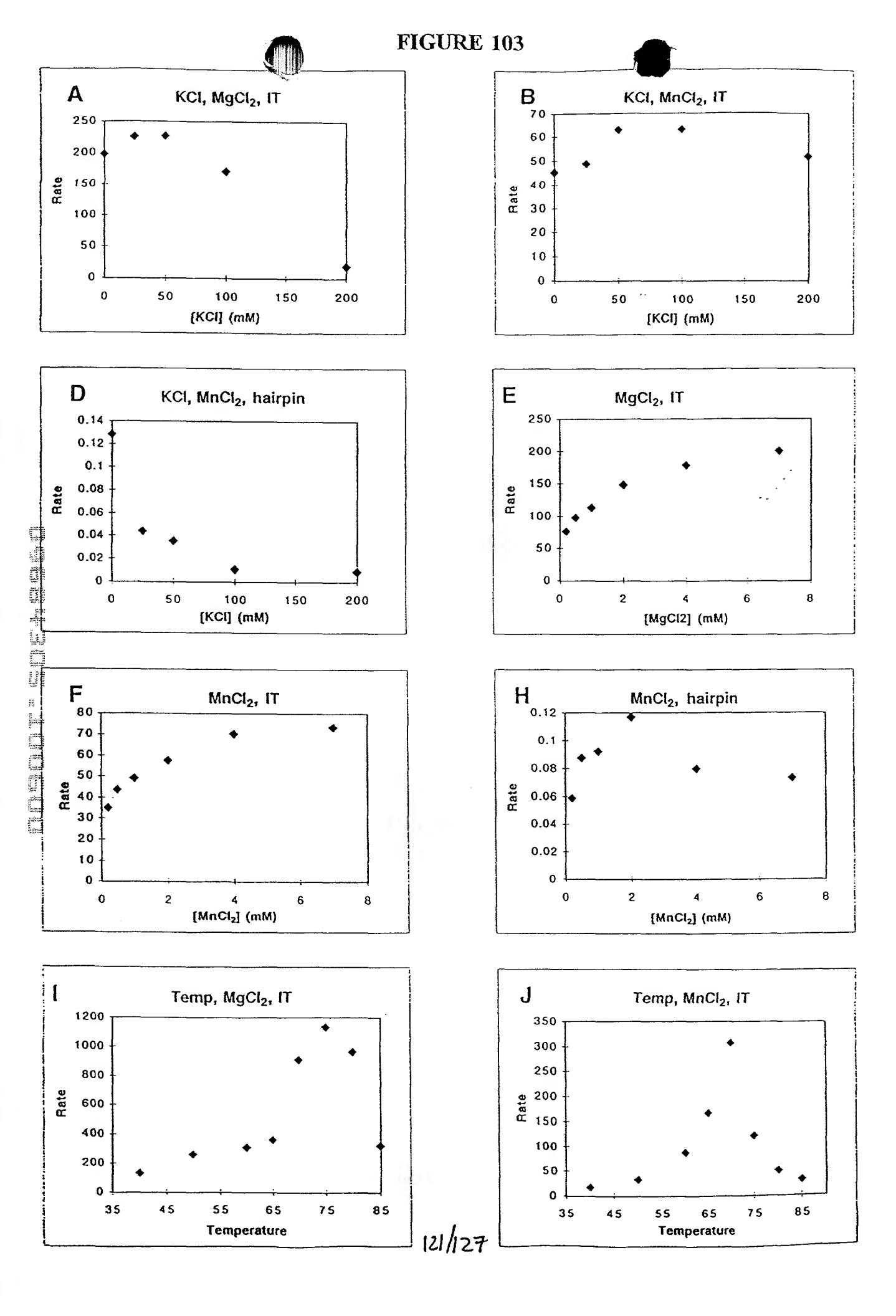
Temperature

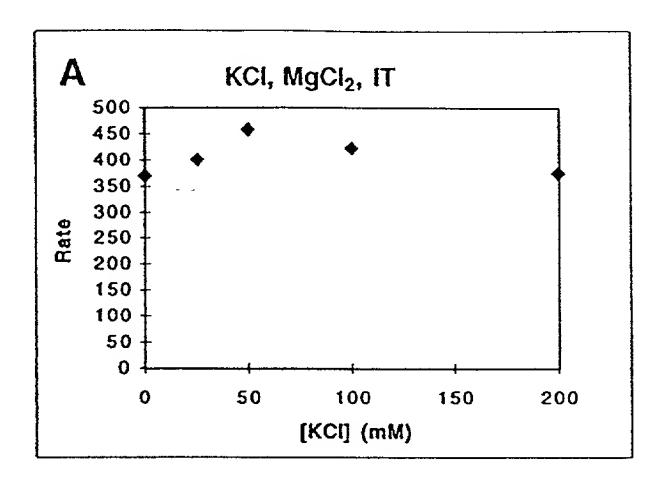
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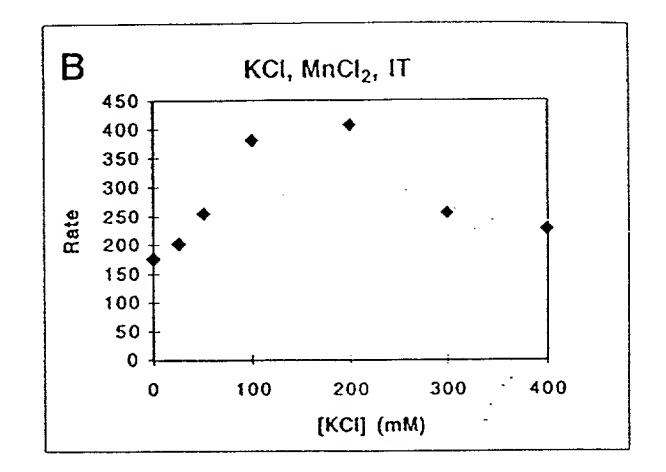
M The state of the

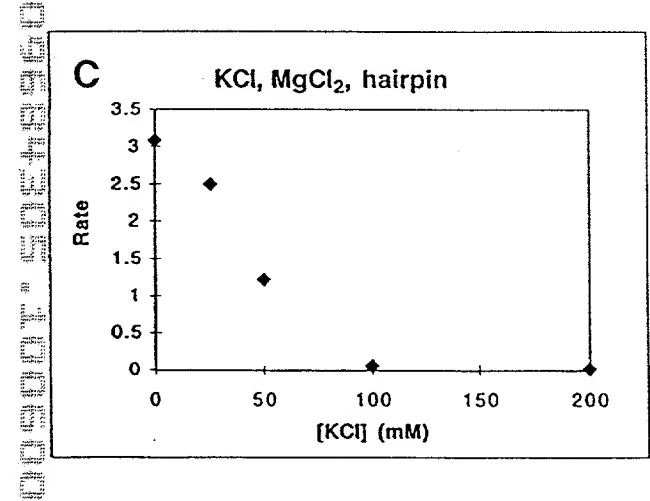
THE THE PARTY OF T

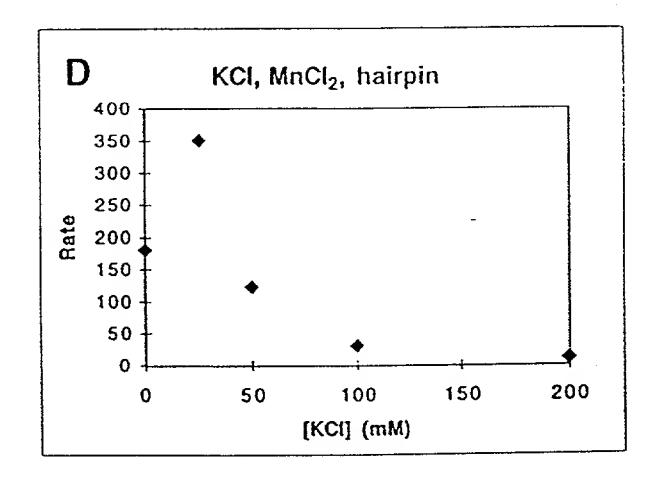
Temperature

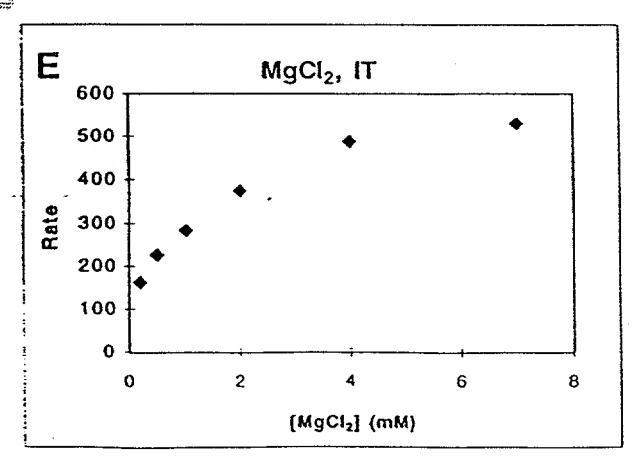












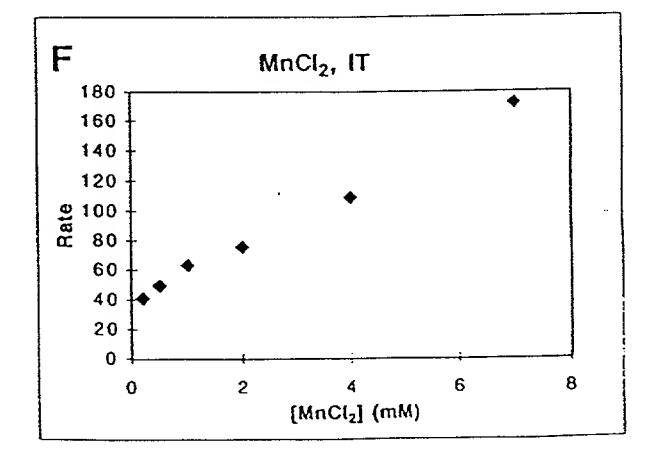
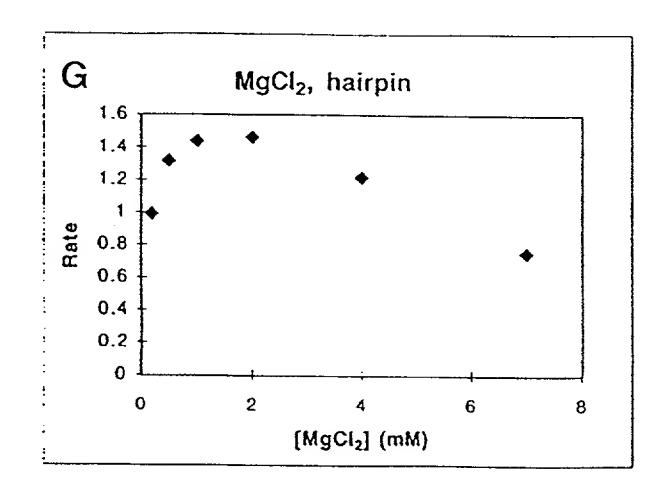
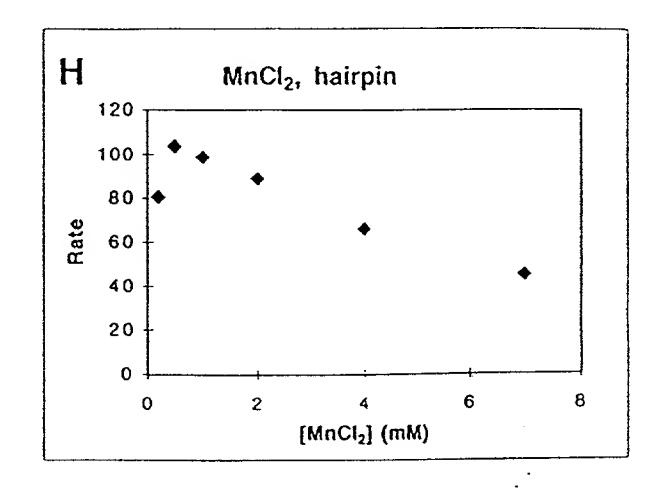
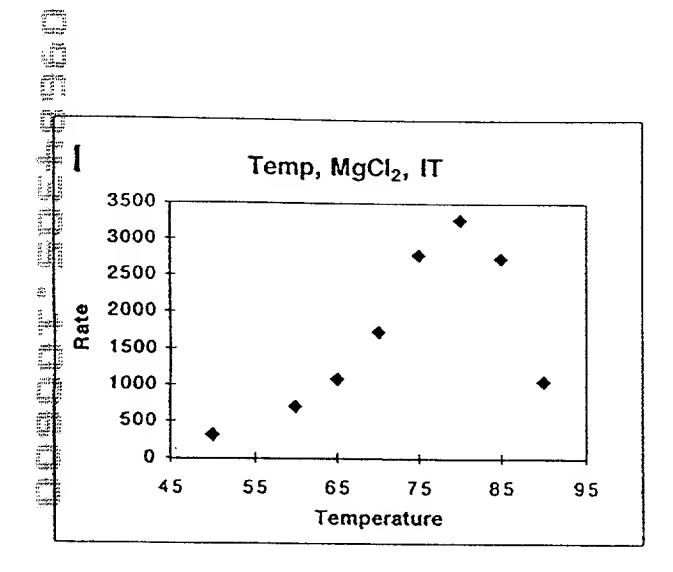
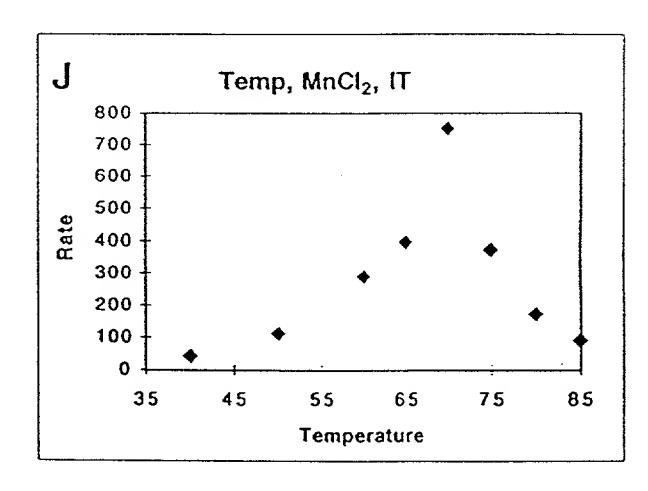


FIGURE 104 (cont.)

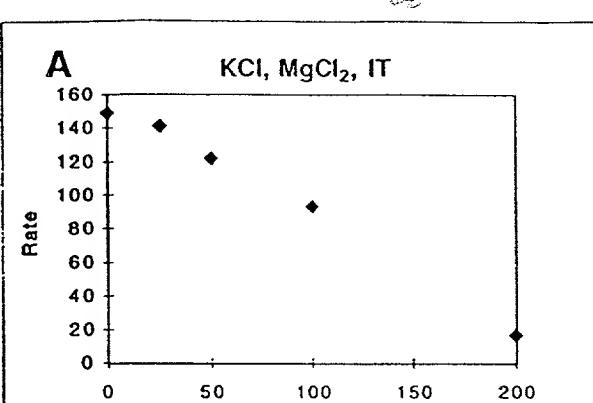




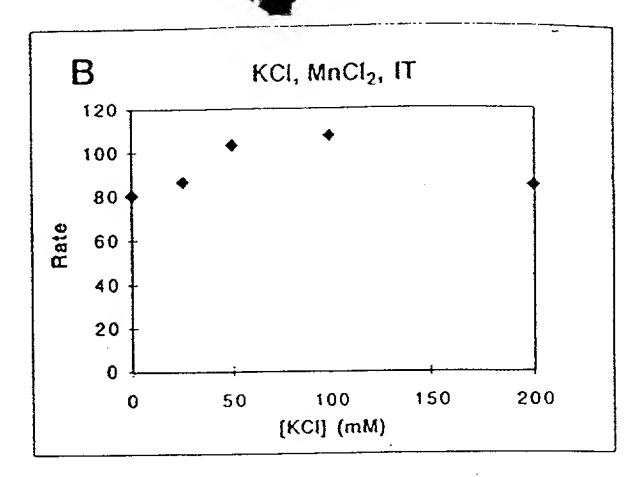


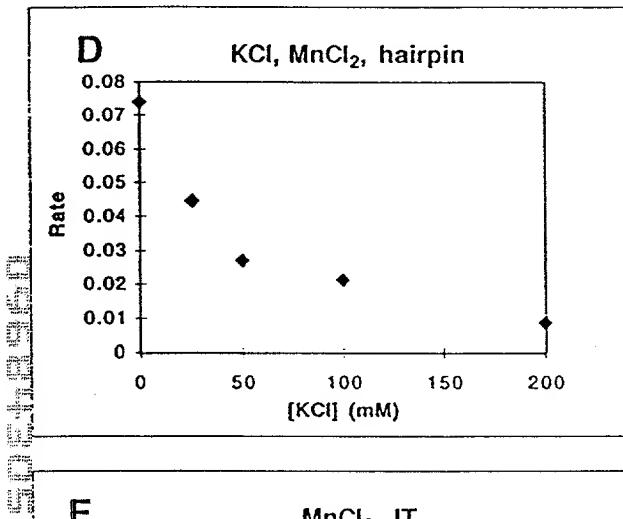


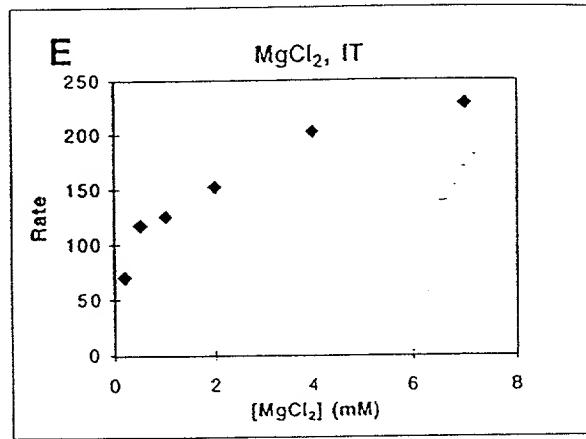


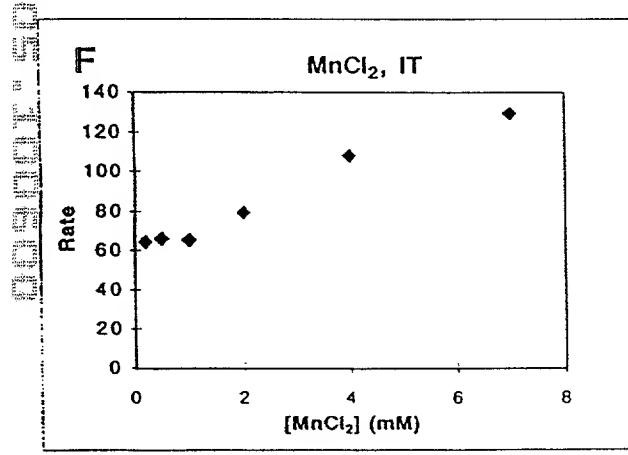


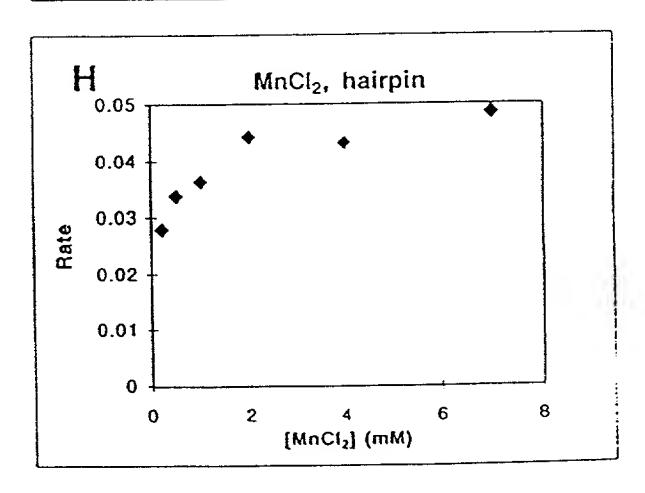
[KCI] (mM)

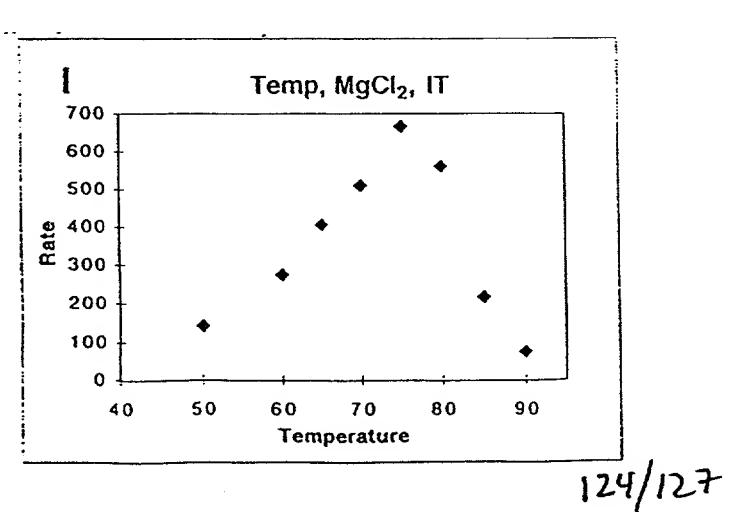


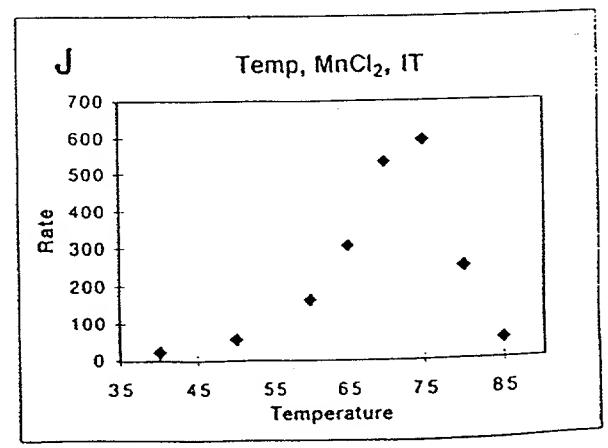




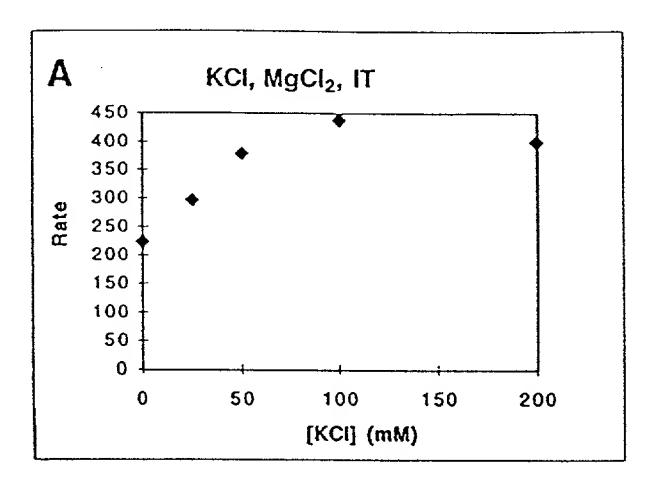


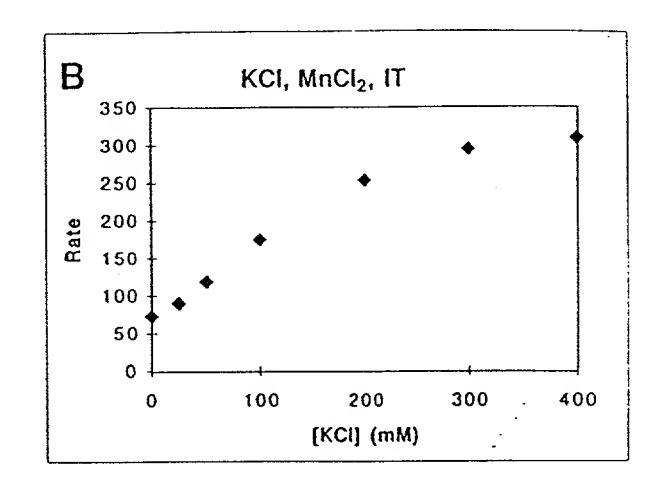


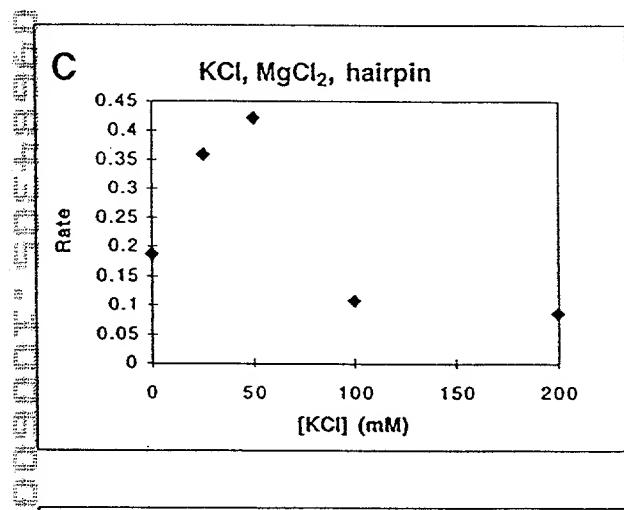


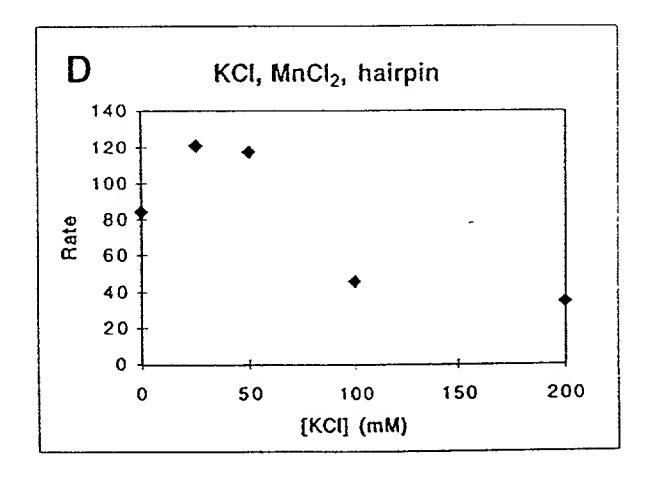


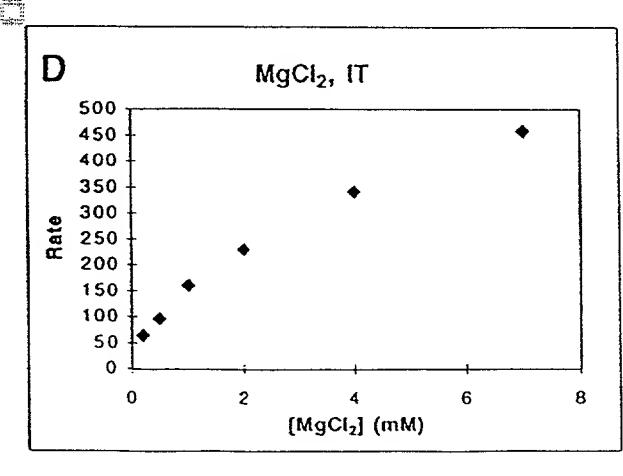


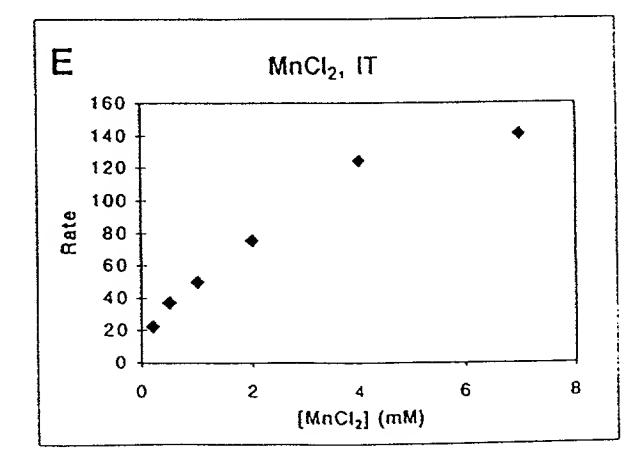




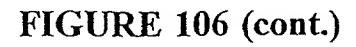


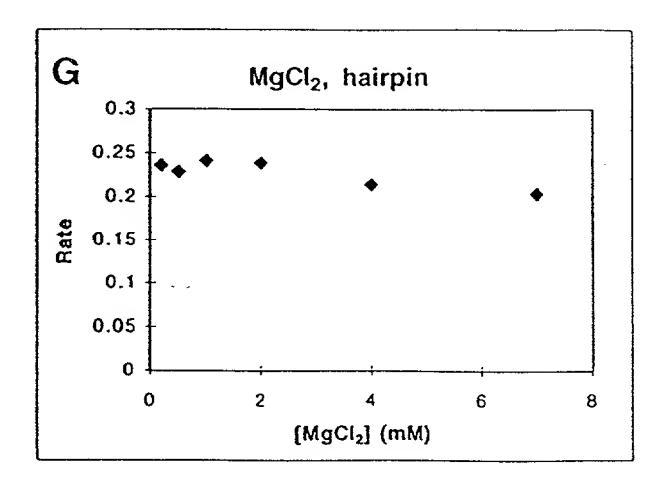


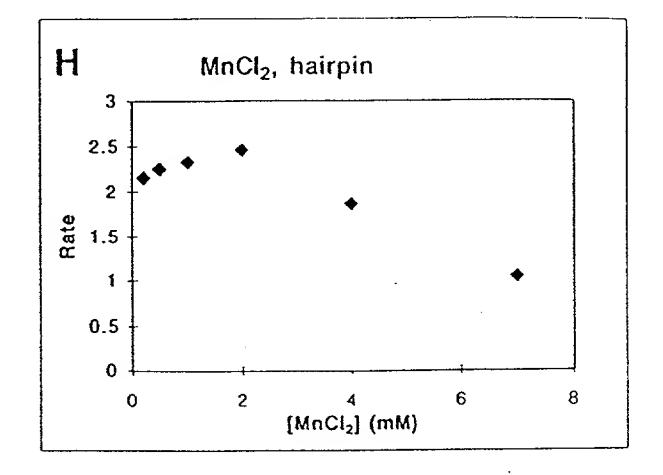


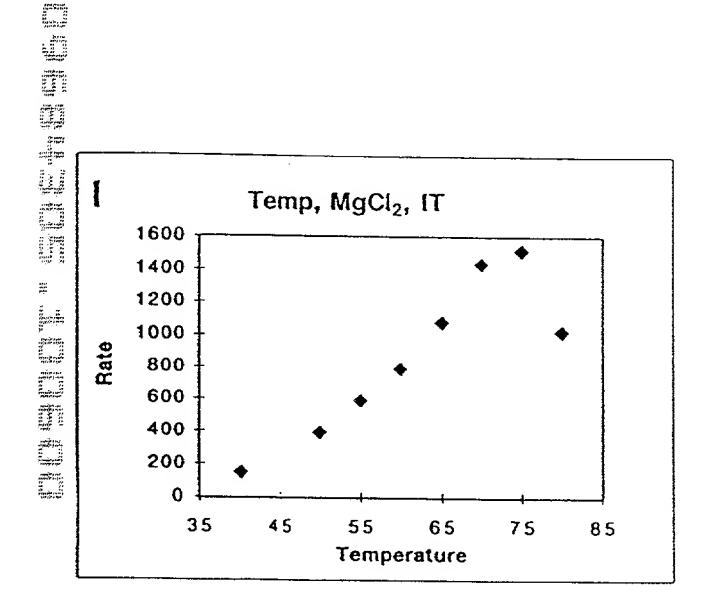


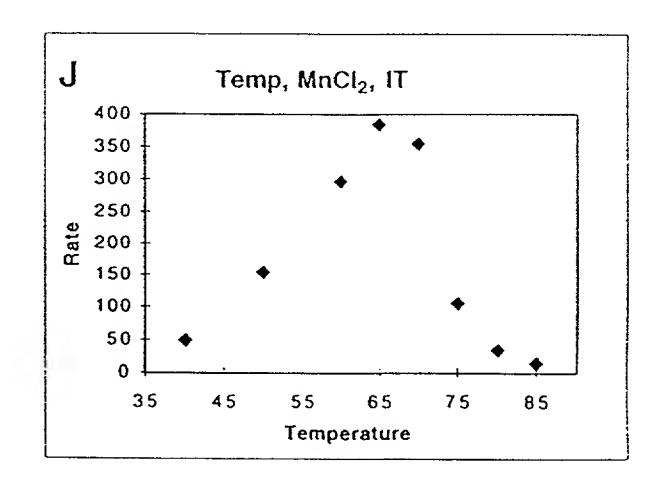












Hairpin Substrate

(A

5 'FI-TTTT CGCTGTCTCGCT A

CGCTGTCTCGCT A

3 'TTT GCGACAGAGCGA A

25-65-1

B) Invader (IT) substrate

5 ' FI-TTT TY A ACGAGCGTCTTT G CGCTGTCTCGCT GA TGCTCGCAGAAA — GCGACAGAGCGA A 25-184-5